PB90-247669

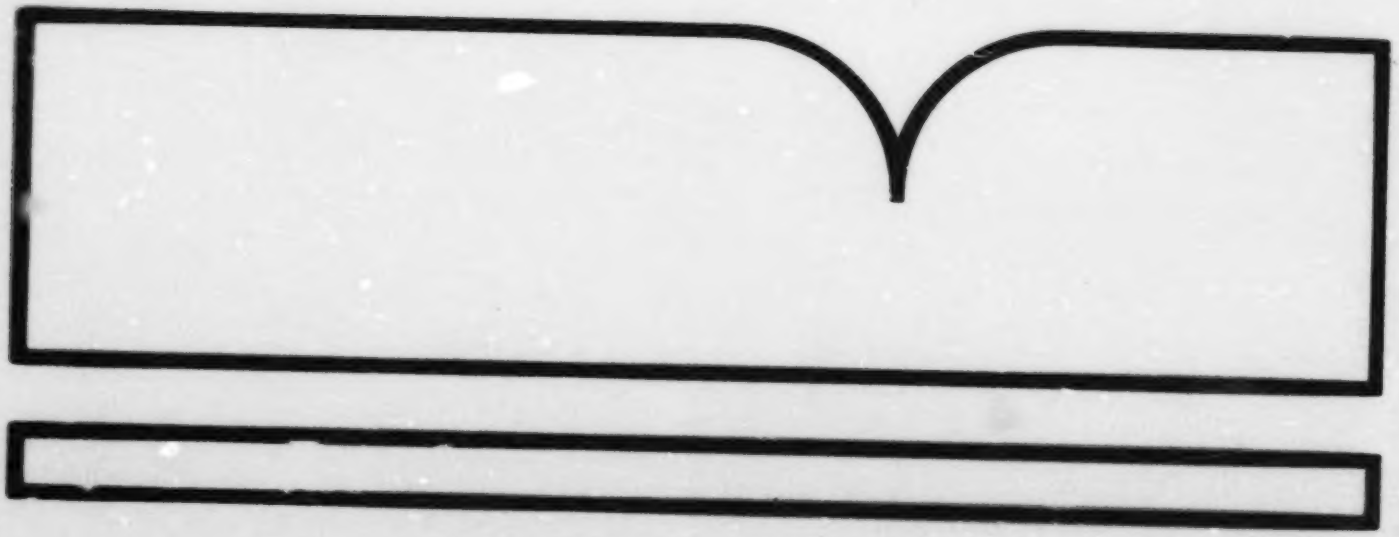
Toxicological Profile for Benz(a)Anthracene

ICF-Clement, Washington, DC

Prepared for:

Agency for Toxic Substances and Disease Registry, Atlanta, GA

Mar 90



U.S. Department of Commerce
National Technical Information Service
NTIS

50272-101

REPORT DOCUMENTATION PAGE	1. REPORT NO. ATSDR/TP-88/4	2.	3. PB90-247669
4. Title and Subtitle: Toxicological Profile for Benzo(a)Anthracene			5. Report Date
			6.
7. Author(s): ATSDR			8. Performing Organization Rept. No. ATSDR/TP-88/ 4
9. Performing Organization Name and Address: Agency for Toxic Substances and Disease Registry (ATSDR), 1600 Clifton Road, N.E., Atlanta, Georgia 30333, in collaboration with U.S. Environmental Protection Agency (EPA)			10. Project/Task/Work Unit No.
			11. Contract(C) or Grant(G) No. (C) 68-02-4235 (G)
12. Sponsoring Organization Name and Address: Agency for Toxic Substances and Disease Registry (ATSDR), 1600 Clifton Road, N.E., Atlanta, Georgia 30333			13. Type of Report & Period Covered: Final
			14.

15. Supplementary Notes

This report was prepared as required by section 110 (3) of the Superfund Amendments and Reauthorization Act of 1986 (42 U.S.C. 9618(f)

16. Abstract (Limit: 200 words)

The ATSDR Toxicological Profile for Benzo(a)anthracene is intended to characterize succinctly the toxicological and health effects information for the substance. It identifies and reviews the key literature that describes the substances's toxicological properties. Other literature is presented but described in less detail. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced. The profile begins with a public health statement, which describes in nontechnical language the substance's relevant toxicological properties. Following the statement is material that presents levels of significant human exposure and, where known, significant health effects. The adequacy of information to determine the substance's health effects is described. Research gaps in nontoxic and health effects information are described. Research gaps that are of significance to the protection of public health will be identified in a separate effort. The focus of the document is on health and toxicological information.

17. Document Analysis a. Descriptors

Benzo(a)Anthracene
Environment
Human health effects
Toxicity

b. Identifiers/Open-Ended Terms

Levels of significant human exposure
Profiles
Superfund

c. COSATI Field/Group

18. Availability Statement	19. Security Class (This Report)	21. No. of Pages
No restrictions on distribution Available from NTIS, Springfield, VA 22161	UNCLASSIFIED	
	20. Security Class (This Page) UNCLASSIFIED	22. Price

(See ANSI-Z39.18) See Instructions on Reverse

OPTIONAL FORM 272 (4-77)
(Formerly NTIS-35)
Department of Commerce

PB90-247669

Toxicological Profile for

BENZ [a]ANTHRACENE

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Agency for Toxic Substances and Disease Registry

REPRODUCED BY
U.S. DEPARTMENT OF COMMERCE
NATIONAL TECHNICAL
INFORMATION SERVICE
SPRINGFIELD, VA 22161

ATSDR/TP-88/04

TOXICOLOGICAL PROFILE FOR BENZ[a]ANTHRACENE

Date Published — March 1990

Prepared by:

ICF-Clement
under Contract No. 68-02-4235

for

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Agency for Toxic Substances and Disease Registry (ATSDR)

in collaboration with

U.S. Environmental Protection Agency (EPA)

Technical editing/document preparation by:

Oak Ridge National Laboratory
under
DOE Interagency Agreement No. 1857-B026-A1

DISCLAIMER

Mention of company name or product does not constitute endorsement by the Agency for Toxic Substances and Disease Registry.

FOREWORD

The Superfund Amendments and Reauthorization Act of 1986 (Public Law 99-499) extended and amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). This public law (also known as SARA) directed the Agency for Toxic Substances and Disease Registry (ATSDR) to prepare toxicological profiles for hazardous substances which are most commonly found at facilities on the CERCLA National Priorities List and which pose the most significant potential threat to human health, as determined by ATSDR and the Environmental Protection Agency (EPA). The list of the 100 most significant hazardous substances was published in the *Federal Register* on April 17, 1987.

Section 110 (3) of SARA directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list. Each profile must include the following content:

> "(A) An examination, summary, and interpretation of available toxicological information and epidemiologic evaluations on a hazardous substance in order to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects.
>
> (B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure which present a significant risk to human health of acute, subacute, and chronic health effects.
>
> (C) Where appropriate, an identification of toxicological testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans."

This toxicological profile is prepared in accordance with guidelines developed by ATSDR and EPA. The guidelines were published in the *Federal Register* on April 17, 1987. Each profile will be revised and republished as necessary, but no less often than every three years, as required by SARA.

The ATSDR toxicological profile is intended to characterize succinctly the toxicological and health effects information for the hazardous substance being described. Each profile identifies and reviews the key literature that describes a hazardous substance's toxicological properties. Other literature is presented but described in less detail than the key studies. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced.

Each toxicological profile begins with a public health statement, which describes in nontechnical language a substance's relevant toxicological properties. Following the statement is material that presents levels of significant human exposure and, where known, significant health effects. The adequacy of information to determine a substance's health effects is described in a health effects summary. Research gaps in toxicologic and health effects information are described in the profile. Research gaps that are of significance to protection of public health will be identified by ATSDR, the National Toxicology Program of the Public Health Service, and EPA. The focus of the profiles is on health and toxicological information; therefore, we have included this information in the front of the document.

The principal audiences for the toxicological profiles are health professionals at the federal, state, and local levels, interested private sector organizations and groups, and members of the public. We plan to revise these documents in response to public comments and as additional data become available; therefore, we encourage comment that will make the toxicological profile series of the greatest use.

This profile reflects our assessment of all relevant toxicological testing and information that has been peer reviewed. It has been reviewed by scientists from ATSDR, EPA, the Centers for Disease Control, and the National Toxicology Program. It has also been reviewed by a panel of nongovernment peer reviewers and was made available for public review. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.

James O. Mason

James O. Mason, M.D., Dr. P.H.
Assistant Surgeon General
Administrator, ATSDR

CONTENTS

FOREWORD iii

LIST OF FIGURES ix

LIST OF TABLES xi

1. PUBLIC HEALTH STATEMENT 1
   - 1.1 WHAT IS BENZ[a]ANTHRACENE? 1
   - 1.2 HOW MIGHT I BE EXPOSED TO BENZ[a]ANTHRACENE? 1
   - 1.3 HOW DOES BENZ[a]ANTHRACENE GET INTO MY BODY? 2
   - 1.4 HOW CAN BENZ[a]ANTHRACENE AFFECT MY HEALTH? 2
   - 1.5 IS THERE A MEDICAL TEST TO DETERMINE IF I HAVE BEEN EXPOSED TO BENZ[a]ANTHRACENE 2
   - 1.6 WHAT LEVELS OF EXPOSURE HAVE RESULTED IN HARMFUL HEALTH EFFECTS? 2
   - 1.7 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH? 3

2. HEALTH EFFECTS SUMMARY 5
   - 2.1 INTRODUCTION 5
   - 2.2 LEVELS OF SIGNIFICANT EXPOSURE 6
     - 2.2.1 Key Studies and Graphical Presentations 6
       - 2.2.1.1 Inhalation exposure 6
       - 2.2.1.2 Oral exposure 7
       - 2.2.1.3 Dermal exposure 7
     - 2.2.2 Biological Monitoring 12
     - 2.2.3 Environmental Levels as Indicators of Exposure and Effects 13
       - 2.2.3.1 Levels found in the environment 13
       - 2.2.3.2 Human exposure potential 13
   - 2.3 ADEQUACY OF DATABASE 14
     - 2.3.1 Introduction 14
     - 2.3.2 Health Effect End Points 14
       - 2.3.2.1 Introduction and graphic summary 14
       - 2.3.2.2 Description of highlights of graphs 17
       - 2.3.2.3 Summary of relevant ongoing research 17

2.3.3 Other Information Needed for Human Health Assessment 18
2.3.3.1 Toxicokinetics and mechanisms of action 18
2.3.3.2 Adequacy of data on biological monitoring 18
2.3.3.3 Environmental considerations 18

3. CHEMICAL AND PHYSICAL INFORMATION 21
3.1 CHEMICAL IDENTITY 21
3.2 PHYSICAL AND CHEMICAL PROPERTIES 21

4. TOXICOLOGICAL DATA 25
4.1 OVERVIEW 25
4.2 TOXICOKINETICS 25
4.2.1 Overview 25
4.2.2 Absorption 26
4.2.2.1 Inhalation 26
4.2.2.2 Oral 26
4.2.2.3 Dermal 26
4.2.3 Distribution 27
4.2.4 Metabolism 27
4.2.5 Excretion 27
4.3 TOXICITY 29
4.3.1 Lethality and Decreased Longevity 29
4.3.2 Systemic/Target Organ Toxicity 29
4.3.3 Reproductive and Developmental Toxicity 29
4.3.4 Genotoxicity 29
4.3.4.1 Overview 29
4.3.4.2 General discussion 33
4.3.5 Carcinogenicity 34
4.3.5.1 Overview 34
4.3.5.2 Inhalation 34
4.3.5.3 Oral 34
4.3.5.4 Dermal 36
4.3.5.5 General discussion 36
4.4 INTERACTIONS WITH OTHER CHEMICALS 36

5. MANUFACTURE, IMPORT, USE, AND DISPOSAL 41
5.1 OVERVIEW 41
5.2 PRODUCTION 41
5.3 IMPORT 41
5.4 USE 42
5.5 DISPOSAL 42

6. ENVIRONMENTAL FATE 43
6.1 OVERVIEW 43
6.2 RELEASES TO THE ENVIRONMENT 43
6.3 ENVIRONMENTAL FATE 44

7. POTENTIAL FOR HUMAN EXPOSURE 47
7.1 OVERVIEW 47
7.2 LEVELS MONITORED IN THE ENVIRONMENT 47
7.2.1 Air 47
7.2.2 Water 47
7.2.3 Soil 48
7.2.4 Food 48
7.2.5 Cigarette Smoke 48
7.3 OCCUPATIONAL EXPOSURES 48
7.4 POPULATIONS AT HIGH RISK 49

8. ANALYTICAL METHODS 51
8.1 ENVIRONMENTAL SAMPLES 51
8.2 BIOLOGICAL SAMPLES 53

9. REGULATORY AND ADVISORY STATUS 57
9.1 INTERNATIONAL 57
9.2 NATIONAL 57
9.2.1 Regulatory Standards 57
9.2.2 Advisory Levels 59
9.2.2.1 Air advisory levels 59
9.2.2.2 Water advisory levels 59
9.2.2.3 Food advisory levels 59
9.2.2.4 Other guidance 60
9.2.3 Data Analysis 60
9.2.3.1 Carcinogenic potency 60
9.3 STATE 60

10. REFERENCES 61

11. GLOSSARY 77

APPENDIX: PEER REVIEW 81

LIST OF FIGURES

2.1 Effects of benz[a]anthracene--oral exposure 8

2.2 Levels of significant exposure for benz[a]anthracene--oral 9

2.3 Effects of benz[a]anthracene--dermal exposure 10

2.4 Levels of significant exposure for benz[a]anthracene--dermal 11

2.5 Availability of information on health effects of benz[a]anthracene (human data) 15

2.6 Availability of information on health effects of benz[a]anthracene (animal data) 16

4.1 Metabolic fate of benz[a]anthracene 28

LIST OF TABLES

3.1 Chemical identity of benz[a]anthracene 22

3.2 Physical and chemical properties of benz[a]anthracene 23

4.1 Genetic toxicity of benz[a]anthracene (in vitro) 30

4.2 Genetic toxicity of benz[a]anthracene (in vivo) 32

4.3 Tumorigenic effects of benz[a]anthracene following administration by gavage 35

4.4 Carcinogenic activity of benz[a]anthracene on mouse skin 37

8.1 Methods for analysis of benz[a]anthracene in environmental media 52

8.2 Methods for analysis of PAHs in biological samples 54

9.1 Regulatory standards and advisory levels 58

1. PUBLIC HEALTH STATEMENT

1.1 WHAT IS BENZ[a]ANTHRACENE?

Benz[a]anthracene (B[a]A) is one of the polycyclic aromatic hydrocarbon (PAH) compounds. Because it is formed when gasoline, garbage, or any animal or plant material burns, it is usually found in smoke and soot. This chemical combines with dust particles in the air and is carried into water and soil and onto crops. Benz[a]anthracene is found in the coal tar pitch that industry uses to join electrical parts together. It is also found in creosote, a chemical used to preserve wood.

1.2 HOW MIGHT I BE EXPOSED TO BENZ[a]ANTHRACENE?

People may be exposed to B[a]A from environmental sources such as air, water, and soil and from cigarette smoke and cooked food. Workers who handle or are involved in the manufacture of PAH-containing materials may also be exposed to B[a]A. Typically, exposure for workers and the general population is not to B[a]A alone but to a mixture of similar chemicals.

The general population may be exposed to dust, soil, and other particles that contain B[a]A. The largest sources of B[a]A in the air are open burning and home heating with wood and coal. Factories that produce coal tar also contribute small amounts of B[a]A to the air. People may come in contact with B[a]A from soil on or near hazardous waste sites, such as former gas-manufacturing sites or abandoned wood-treatment plants that used creosote. At this time, B[a]A has been found at 62 out of 1,177 sites on the National Priorities List (NPL) of hazardous waste sites in the United States. As more sites are evaluated by the Environmental Protection Agency (EPA), this number could change. The soil near areas where coal, wood, or other products have been burned is another source of exposure. Exposure to B[a]A and other PAHs may also occur through skin contact with products that contain PAHs such as creosote-treated wood, asphalt roads, or coal tar.

People may be exposed to B[a]A by drinking water from the drinking water supplies in the U.S. that have been found to contain low levels of the chemical. Foods grown in contaminated soil or air may contain B[a]A. Cooking food at high temperatures, as occurs during charcoal-grilling or charring, can increase the amount of B[a]A in the food. Benz[a]anthracene has been found in cereals, vegetables, fruits, meats, beverages, and in cigarette smoke.

The greatest exposure to B[a]A is likely to take place in the workplace. People who work in coal tar production plants; coking plants; asphalt production plants; coal-gasification sites; smoke houses; municipal trash incinerators; and facilities that burn wood, coal, or

oil may be exposed to B[a]A in the workplace air. Benz[a]anthracene may also be found in areas where high-temperature food fryers and broilers are used.

1.3 HOW DOES BENZ[a]ANTHRACENE GET INTO MY BODY?

The most common way B[a]A enters the body is through the lungs when a person breathes in air or smoke containing it. It also enters the body through the digestive system when substances containing it are swallowed. Although B[a]A does not normally enter the body through the skin, small amounts could enter if contact occurs with soil that contains high levels of B[a]A (for example, near a hazardous waste site) or if contact is made with heavy oils containing B[a]A.

1.4 HOW CAN BENZ[a]ANTHRACENE AFFECT MY HEALTH?

Benz[a]anthracene causes cancer in laboratory animals when applied to their skin. This finding suggests that it is likely that people exposed in the same manner could also develop cancer.

Because studies of B[a]A are not complete, we don't know if B[a]A that is breathed in or swallowed could cause cancer or if it can cause harmful effects other than cancer.

1.5 IS THERE A MEDICAL TEST TO DETERMINE IF I HAVE BEEN EXPOSED TO BENZ[a]ANTHRACENE?

Very few tests are available that can tell if exposure to B[a]A has taken place. In the body, B[a]A is changed to related chemical substances called metabolites. The metabolites can bind with DNA, the genetic material of the body. The body's response after exposure can be measured in the blood. However, this test is still being developed. Benz[a]anthracene can also be found in the urine of individuals exposed to PAHs. It is not possible to know from these tests how much B[a]A a person was exposed to or to predict what health effects may happen at certain levels. Also, none of these tests have been used in exposure situations outside the workplace.

1.6 WHAT LEVELS OF EXPOSURE HAVE RESULTED IN HARMFUL HEALTH EFFECTS?

No information has been found about specific levels of B[a]A that have caused harmful effects in people after breathing, swallowing, or touching the substance.

Skin cancer has developed in mice that had B[a]A on their skin throughout their lives. Skin cancer is the only harmful effect that can be predicted when animals are exposed to B[a]A. It is not known if similar levels could cause cancer in people. No information has been found about harmful effects of B[a]A in animals that breathed in or ate the chemical.

1.7. WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?

Based on information from another PAH chemical, the federal government has developed standards and guidelines to protect individuals from the potential health effects of PAHs, including B[a]A, in drinking water. EPA has provided estimates of levels of total cancer-causing PAHs in lakes and streams associated with various risks of developing cancer in people. EPA has also determined that any release of PAHs of more than 1 pound should be reported to the National Response Center.

Pure B[a]A is produced in the United States only as a laboratory chemical. However, B[a]A is a PAH, and PAHs are found in coal tar and in the creosote oils and pitches formed from the production of coal tar. The government's goal has been to protect workers involved with the production of coal tar products. Although government standards are not for B[a]A alone, they are useful in controlling exposure to total PAHs.

The National Institute for Occupational Safety and Health (NIOSH) has determined that workplace exposure to coal products can increase the risk of lung and skin cancer in workers and suggests a workplace exposure limit for coal tar products of 0.1 milligram of PAHs per cubic meter of air (0.1 mg/m^3) for a 10-hour workday, 40-hour workweek. NIOSH has not suggested a specific workplace limit for B[a]A. The Occupational Safety and Health Administration (OSHA) has set a legal limit of 0.2 milligram of all PAHs per cubic meter of air (0.2 mg/m^3).

2. HEALTH EFFECTS SUMMARY

2.1 INTRODUCTION

This section summarizes and graphs data on the health effects concerning exposure to B[a]A. The purpose of this section is to present levels of significant exposure for B[a]A based on key toxicological studies, epidemiological investigations, and environmental exposure data. The information presented in this section is critically evaluated and discussed in Sect. 4, Toxicological Data, and Sect. 7, Potential for Human Exposure.

This Health Effects Summary section comprises two major parts. Levels of Significant Exposure (Sect. 2.2) presents brief narratives and graphics for key studies in a manner that provides public health officials, physicians, and other interested individuals and groups with (1) an overall perspective of the toxicology of B[a]A; and (2) a summarized depiction of significant exposure levels associated with various adverse health effects. This section also includes information on the levels of B[a]A that have been monitored in human fluids and tissues and information about levels of B[a]A found in environmental media and their association with human exposures.

The significance of the exposure levels shown on the graphs may differ depending on the user's perspective. For example, physicians concerned with the interpretation of overt clinical findings in exposed persons or with the identification of persons with the potential to develop such disease may be interested in levels of exposure associated with frank effects (Frank Effect Level, FEL). Public health officials and project managers concerned with response actions at Superfund sites may want information on levels of exposure associated with more subtle effects in humans or animals (Lowest-Observed-Adverse-Effect Level, LOAEL) or exposure levels below which no adverse effects (No-Observed-Adverse-Effect Level, NOAEL) have been observed. Estimates of levels posing minimal risk to humans (Minimal Risk Levels) are of interest to health professionals and citizens alike.

Adequacy of Database (Sect. 2.3) highlights the availability of key studies on exposure to B[a]A in the scientific literature and displays these data in three-dimensional graphs consistent with the format in Sect. 2.2. The purpose of this section is to suggest where there might be insufficient information to establish levels of significant human exposure. These areas will be considered by the Agency for Toxic Substances and Disease Registry (ATSDR), EPA, and the National Toxicology Program (NTP) of the U.S. Public Health Service in order to develop a research agenda for benz[a]anthracene.

2.2 LEVELS OF SIGNIFICANT EXPOSURE

2.2.1 Key Studies and Graphical Presentations

To help public health professionals address the needs of persons living or working near hazardous waste sites, the toxicology data summarized in this section are organized first by route of exposure--inhalation, ingestion, and dermal--and then by toxicological end points that are categorized into six general areas--lethality, systemic/target organ toxicity, developmental toxicity, reproductive toxicity, genetic toxicity, and carcinogenicity. The data are discussed in terms of three exposure periods--acute, intermediate, and chronic.

Two kinds of graphs are used to depict the data. The first type is a "thermometer" graph. It provides a graphical summary of the human and animal toxicological end points and levels of exposure for each exposure route for which data are available. The ordering of effects does not reflect the exposure duration or species of animal tested. The second kind of graph shows Levels of Significant Exposure (LSE) for each route and exposure duration. The points on the graph showing NOAELs and LOAELs reflect the actual doses (levels of exposure) used in the key studies. No adjustments for exposure duration or intermittent exposure protocol were made.

Adjustments reflecting the uncertainty of extrapolating animal data to man, intraspecies variations, and differences between experimental vs actual human exposure conditions were considered when estimates of levels posing minimal risk to human health were made for noncancer end points. These minimal risk levels were derived for the most sensitive noncancer end point for each exposure duration by applying uncertainty factors. These levels are shown on the graphs as a broken line starting from the actual dose (level of exposure) and ending with a concave-curved line at its terminus. Although methods have been established to derive these minimal risk levels (Barnes et al. 1987), shortcomings exist in the techniques that reduce the confidence in the projected estimates. Also shown on the graphs under the cancer end point are low-level risks (10^{-4} to 10^{-7}) reported by EPA if available. In addition, the actual dose (level of exposure) associated with the tumor incidence is plotted.

2.2.1.1 Inhalation exposure

No information could be located in the available literature concerning the effects of B[a]A following inhalation exposure.

Lethality and decreased longevity. No information is available.

Systemic toxicity. No information is available.

Developmental toxicity. No information is available.

Reproductive toxicity. No information is available.

Genotoxicity. No information is available.

Carcinogenicity. No reports directly correlating inhalation exposure to B[a]A and cancer induction are available, although reports

of cancer among individuals exposed to mixtures of PAHs containing B[a]A may lend some qualitative support to its potential for carcinogenicity in humans.

2.2.1.2 Oral exposure

Some information was located in the available literature on the effects of B[a]A following oral exposure. Two studies exist in which B[a]A was administered by gavage; however, they were judged to be inadequate to support the development of significant human exposure levels for the purposes of this document. These studies do provide some evidence for the carcinogenic potential of B[a]A by this route, however. The dose at which an increase in benign tumor incidence was observed is depicted graphically in Figs. 2.1 and 2.2.

Lethality and decreased longevity. No information is available.

Systemic toxicity. No information is available.

Developmental toxicity. No information is available.

Reproductive toxicity. No information is available.

Genotoxicity. Information is only available on insects, e.g., *Drosophila melanogaster*. Results were negative in these studies (Fahmy and Fahmy 1973, 1980; Zijlstra and Vogel 1984).

Carcinogenicity. No information is available on the carcinogenicity of B[a]A in humans following oral exposure.

Two studies were located in which elevated numbers of benign tumors were found in animals administered B[a]A by stomach tube for intermediate periods of time; however, these studies were flawed and judged to be inadequate to support the development of significant human exposure levels for the purposes of this document, although they provide some evidence for the oral carcinogenicity of B[a]A.

2.2.1.3 Dermal exposure

No information is available on the effects of short-term dermal exposures of humans to B[a]A. There are reports in the literature that B[a]A suppresses the sebaceous glands in mouse skin following topical application (Bock and Mund 1958). However, these studies failed to employ control groups; therefore, definitive conclusions concerning the dermal toxicity of B[a]A cannot be made.

B[a]A has been shown to be carcinogenic following intermediate-term dermal exposure. This conclusion is based on observations in laboratory animals, since no data are available for human exposure; results are summarized in Figs. 2.3 and 2.4.

Lethality and decreased longevity. No information is available.

Systemic toxicity. No information is available.

Developmental toxicity. No information is available.

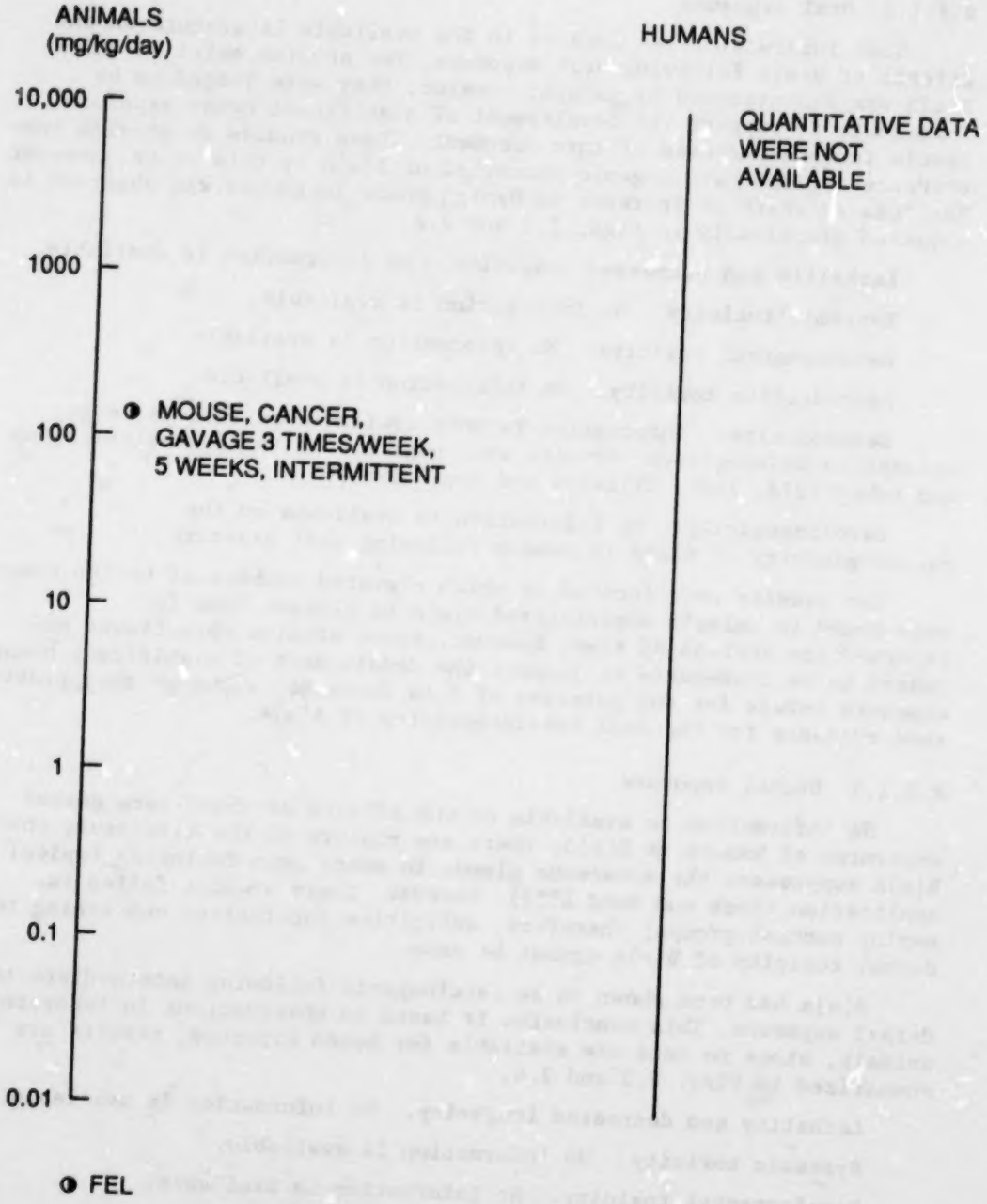


Fig. 2.1. Effects of benz[a]anthracene--oral exposure.

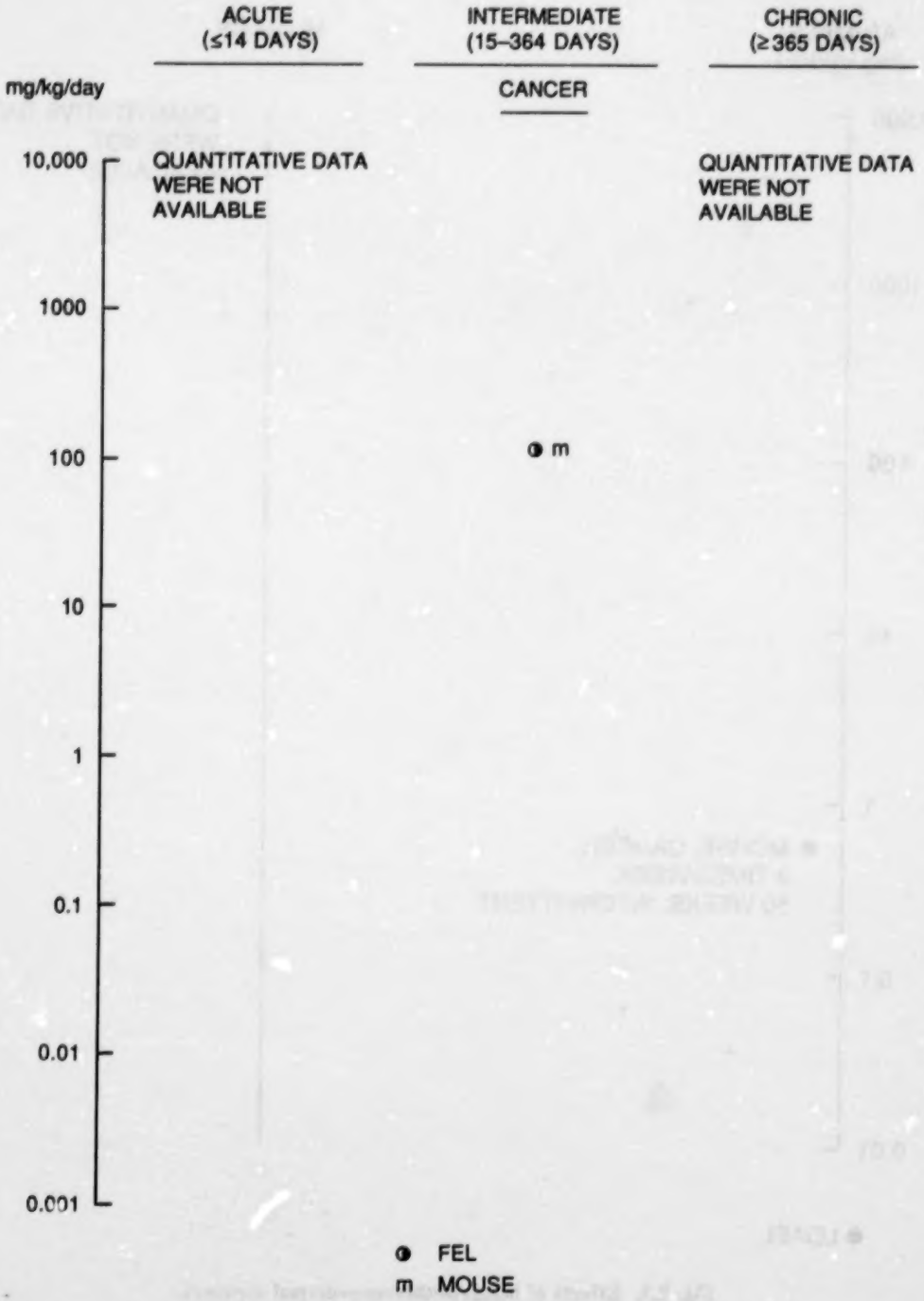


Fig. 2.2. Levels of significant exposure for benz[a]anthracene—oral.

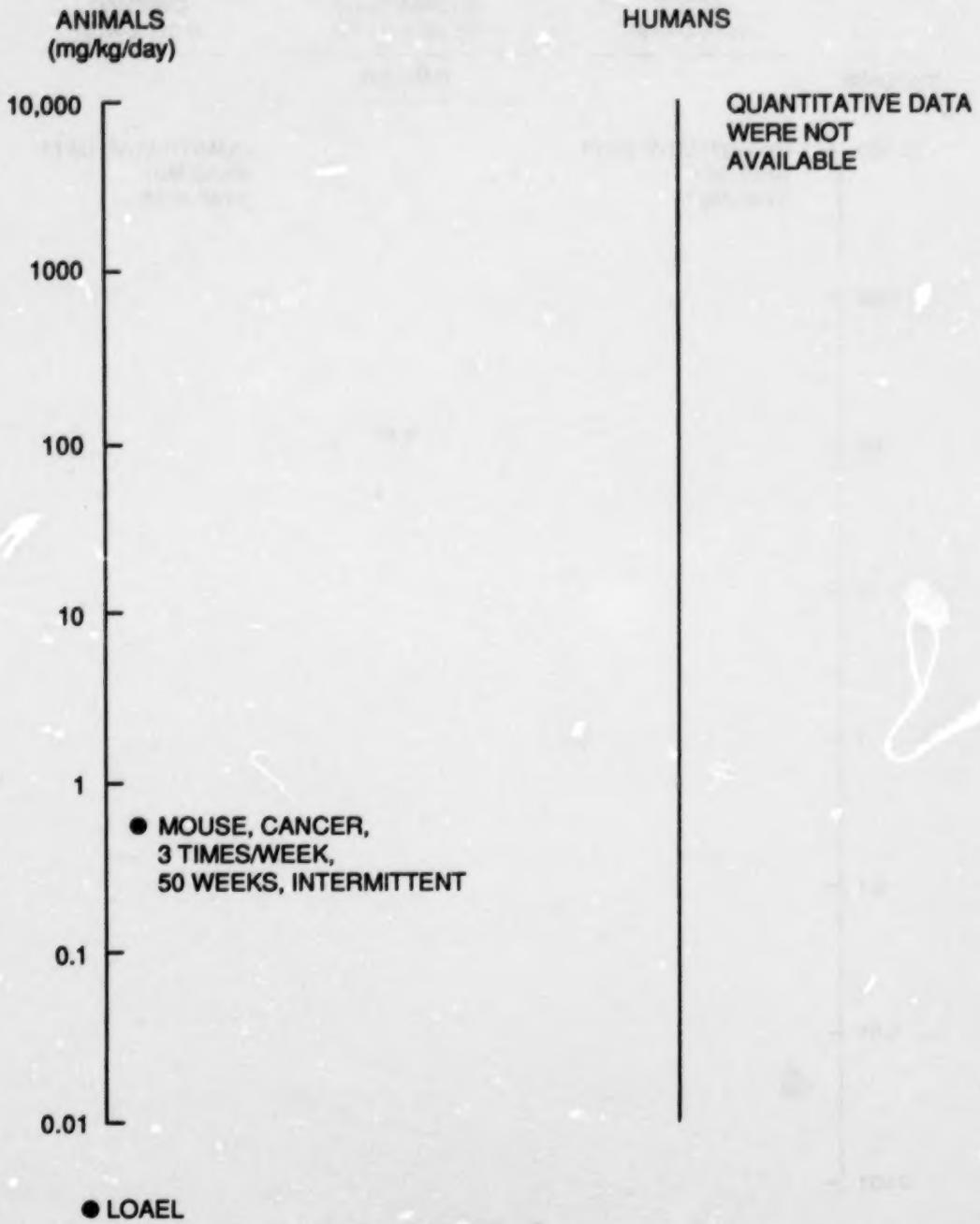


Fig. 2.3. Effects of benz[a]anthracene--dermal exposure.

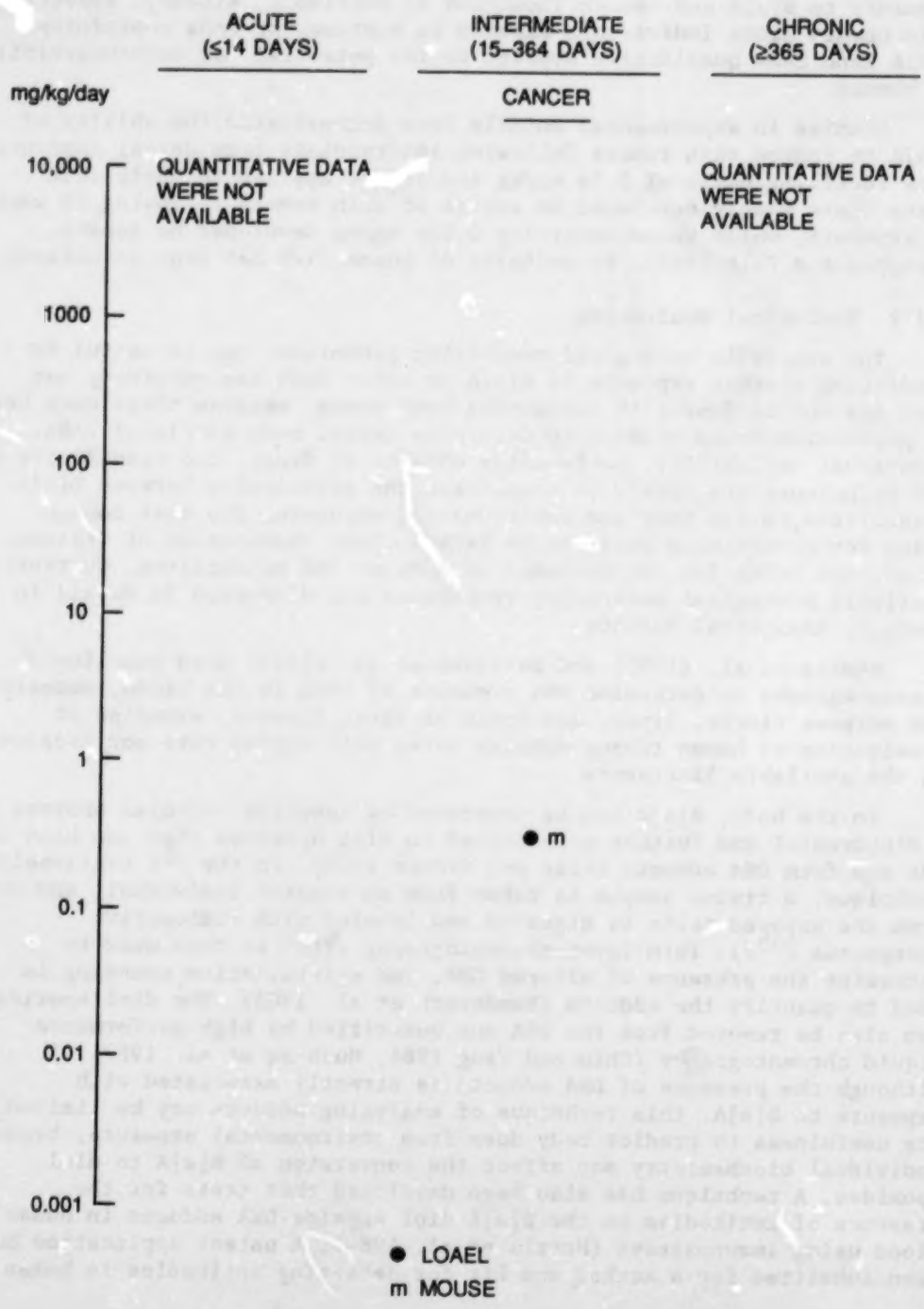


Fig. 2.4. Levels of significant exposure for benz[a]anthracene—dermal.

Reproductive toxicity. No information is available.

Genotoxicity. No information is available.

Carcinogenicity. No information directly correlating human dermal exposure to B[a]A and cancer induction is available, although reports of skin tumors among individuals exposed to mixtures of PAHs containing B[a]A lend some qualitative support to its potential for carcinogenicity in humans.

Studies in experimental animals have demonstrated the ability of B[a]A to induce skin tumors following intermediate-term dermal exposure. Mice receiving doses of 0.34 mg/kg and larger applied to their skin three times weekly developed an excess of skin tumors following 50 weeks of exposure, while those receiving 0.034 mg/kg developed no tumors (Bingham and Falk 1969). No estimate of human risk has been calculated.

2.2.2 Biological Monitoring

The available biological monitoring techniques can be useful in predicting whether exposure to B[a]A or other PAHs has occurred; but they may not be useful in estimating body doses, because there have been no population-based studies to determine normal body levels of PAHs. Individual variability, confounding effects of drugs, and specificity of the techniques are likely to complicate the association between B[a]A metabolites in the body and environmental exposure. The most common tests for determining exposure to PAHs include examination of tissues, blood, and urine for the presence of PAHs or PAH metabolites. Currently available biological monitoring techniques are discussed in detail in Sect. 8, Analytical Methods.

Modica et al. (1982) and Bartosek et al. (1984) used gas-liquid chromatography to determine the presence of PAHs in the blood, mammary and adipose tissue, liver, and brain of rats. However, examples of examination of human tissue samples using this method were not located in the available literature.

In the body, B[a]A can be converted by specific cellular enzymes to a dihydrodiol and further metabolized to diol epoxides that can bind to DNA and form DNA adducts (Sims and Grover 1974). In the ^{32}P postlabeling technique, a tissue sample is taken from an exposed individual, and DNA from the exposed cells is digested and labeled with radioactive phosphorus (^{32}P). Thin-layer chromatography (TLC) is then used to determine the presence of altered DNA, and scintillation counting is used to quantify the adducts (Randerath et al. 1985). The diol epoxides can also be removed from the DNA and quantified by high-performance liquid chromatography (Chiu and Yang 1986, Mushtaq et al. 1987). Although the presence of DNA adducts is directly associated with exposure to B[a]A, this technique of analyzing adducts may be limited in its usefulness to predict body dose from environmental exposure, because individual biochemistry may affect the conversion of B[a]A to diol epoxides. A technique has also been developed that tests for the presence of antibodies to the B[a]A diol epoxide-DNA adducts in human blood using immunoassays (Harris et al. 1986). A patent application has been submitted for a method and kit for detecting antibodies in human

sera to PAH diol epoxide-DNA adducts by immunoassay (Harris 1985). This method has been examined in occupationally exposed individuals and in smokers.

B[a]A has been detected in the urine of individuals occupationally exposed to atmospheric PAHs and in individuals treated with therapeutic coal tar for psoriasis (Becher and Bjorseth 1983, Becher et al. 1984, Clonfero et al. 1986).

A recent technique using an antibody-based fiber-optic biosensor has been tested to detect benzo[a]pyrene. This technique has been investigated in sample solutions containing benzo[a]pyrene and may be useful for assessing an individual's exposure to other PAHs provided appropriate antibodies are used (Vo-Dinh et al. 1987).

2.2.3 Environmental Levels as Indicators of Exposure and Effects

2.2.3.1 Levels found in the environment

B[a]A has been detected in air, water, and soils, but limited information is available to adequately characterize background exposures. B[a]A air concentrations in U.S. cities have been reported in the range of 0.04 to 63 ng/m^3 (Fox and Staley 1976, DeMaio and Corn 1966). B[a]A concentrations in finished drinking waters of the United States have been reported in the range of less than 1 to 2 ng/L (Sorrell et al. 1981). No data are available on B[a]A levels in soil, but concentrations of total PAHs, including B[a]A, have been reported in the range of 4 to 13 mg/kg in relatively rural areas of the United States (summarized by Blumer et al. 1977).

B[a]A may occur in the soil and on particulate matter in the air surrounding waste sites, such as former manufactured-gas plants and creosote wood treatment plants. However, exposure levels at these sites have not yet been published.

Data are not available which relate these levels to significant health effects in humans following environmental exposures.

2.2.3.2 Human exposure potential

Humans may be exposed to B[a]A in air, water, soil, and food, and each of these media constitutes a normal route of background exposures. Background exposures to B[a]A are expected to be at low levels. Much higher exposure concentrations are associated with tobacco smoke and with some occupational environments. At hazardous waste sites, exposure concentrations may also be higher, and humans may be exposed to B[a]A via contact with soil or inhalation of particulate matter in air. Estimates of body doses or tissue levels associated with B[a]A intake require (1) information on the chemical concentrations in soil and air, (2) certain assumptions about factors controlling intake, and (3) information on absorption of B[a]A from soil or particulate matter.

Information on the first two of these data needs is relatively site-specific in nature and cannot be generalized across all sites. Quantitative toxicological information on absorption of B[a]A from soil or particulate matter is lacking, although absorption is expected to be

low (Becher et al. 1984). Consequently, estimates of doses following exposure to B[a]A in soil or air are based on assumptions regarding dermal absorption from soil and absorption of incidentally ingested B[a]A on soil or inhaled B[a]A on particulate matter. These assumptions lend uncertainty to any risk assessment of potential health effects following environmental exposures.

2.3 ADEQUACY OF DATABASE

2.3.1 Introduction

Section 110 (3) of SARA directs the Administrator of ATSDR to prepare a toxicological profile for each of the 100 most significant hazardous substances found at facilities on the CERCLA National Priorities List. Each profile must include the following content:

"(A) An examination, summary, and interpretation of available toxicological information and epidemiologic evaluations on a hazardous substance in order to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects.

(B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure which present a significant risk to human health of acute, subacute, and chronic health effects.

(C) Where appropriate, an identification of toxicological testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans."

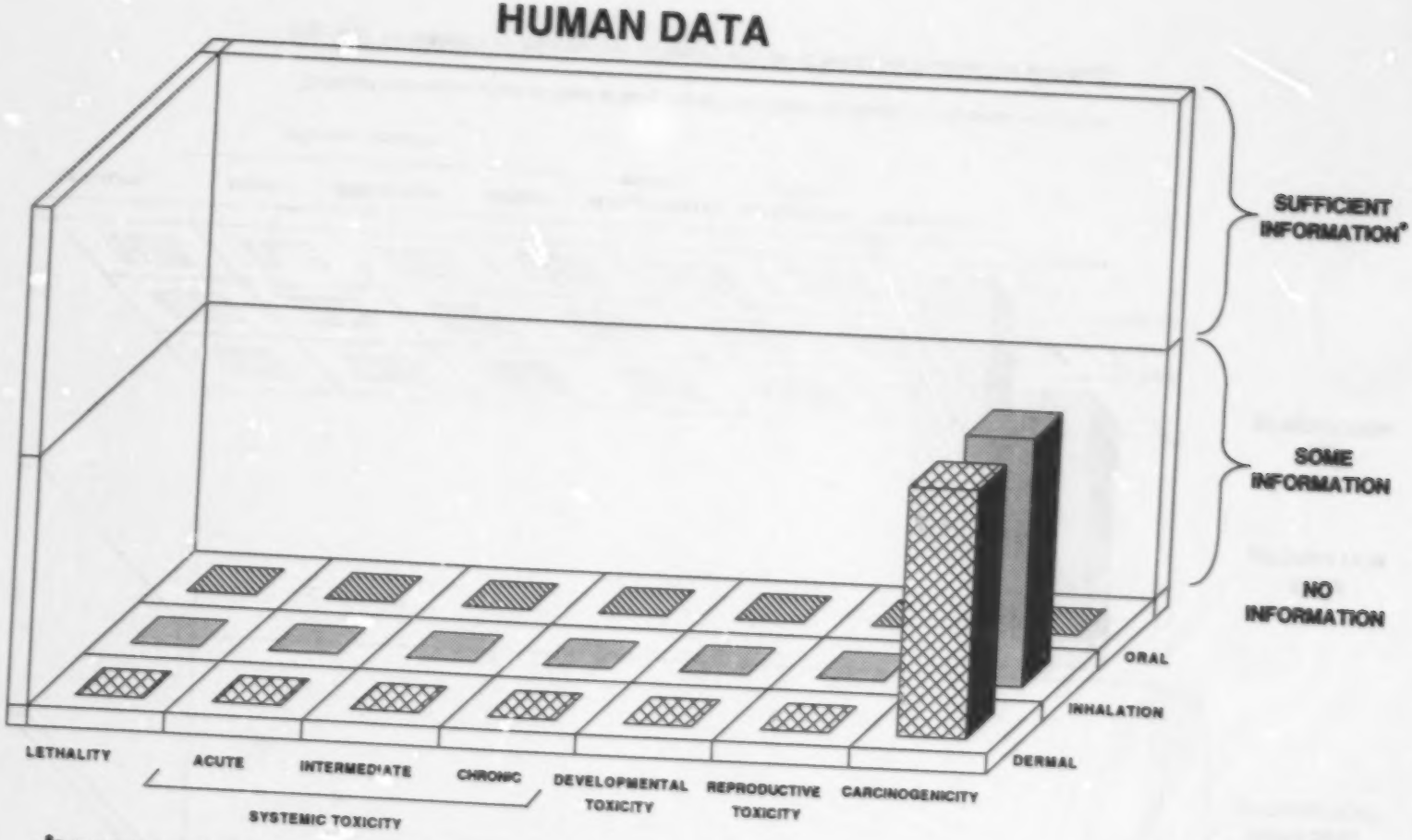
This section identifies gaps in current knowledge relevant to developing levels of significant exposure for B[a]A. Such gaps are identified for certain health effect end points (lethality, systemic/target organ toxicity, developmental toxicity, reproductive toxicity, and carcinogenicity) reviewed in Sect. 2.2 of this profile in developing levels of significant exposure for B[a]A, and for other areas such as human biological monitoring and mechanisms of toxicity. The present section briefly summarizes the availability of existing human and animal data, identifies data gaps, and summarizes research in progress that may fill such gaps.

Specific research programs for obtaining data needed to develop levels of significant exposure for B[a]A will be developed by ATSDR, NTP, and EPA in the future.

2.3.2 Health Effect End Points

2.3.2.1 Introduction and graphic summary

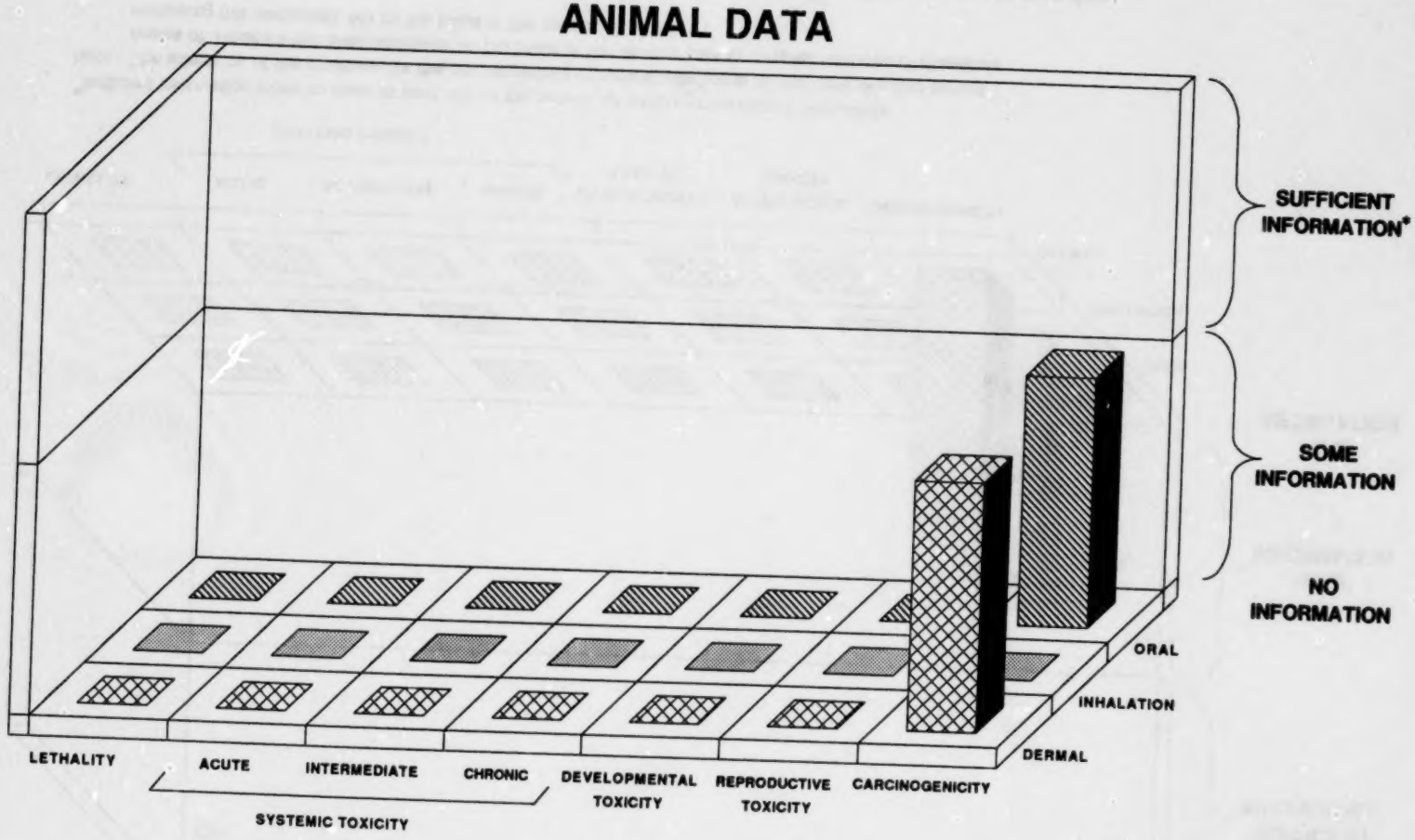
The availability of data for health effects in humans and animals is depicted on bar graphs in Figs. 2.5 and 2.6, respectively.



*Sufficient information exists to meet at least one of the criteria for cancer or noncancer end points.

Note: The adequacy of the database for the carcinogenicity of benz[a]anthracene by the inhalation and dermal routes of exposure has been assessed on the basis of human exposure to complex mixtures of chemicals containing this compound, not on the basis of the compound alone.

Fig. 2.5. Availability of information on health effects of benz[a]anthracene (human data).



*Sufficient information exists to meet at least one of the criteria for cancer or noncancer end points.

Fig. 2.6. Availability of information on health effects of benz[a]anthracene (animal data).

The bars of full height indicate that there are data to meet at least one of the following criteria:

1. For noncancer health end points, one or more studies are available that meet current scientific standards and are sufficient to define a range of toxicity from levels that cause no effects (NOAELs) to levels that cause effects (LOAELs or FELs).
2. For human carcinogenicity, a substance is classified as either a "known human carcinogen" or a "probable human carcinogen" by both EPA and the International Agency for Research on Cancer (IARC) (qualitative), and the data are sufficient to derive a cancer potency factor (quantitative).
3. For animal carcinogenicity, a substance causes a statistically significant number of tumors in at least one species and the data are sufficient to derive a cancer potency factor.
4. There are studies which show that the chemical does not cause this health effect via this exposure route.

Bars of half height indicate that "some" information for the end point exists, but does not meet any of these criteria.

The absence of a column indicates that no information exists for that end point and route.

2.3.2.2 Description of highlights of graphs

Figure 2.5 indicates that there are no data available to assess significant exposure levels of B[a]A for humans. Reports of adverse health effects such as carcinogenicity by the inhalation and dermal routes of exposure do exist for mixtures of chemicals that include B[a]A, providing some information to qualitatively assess the role of B[a]A as a human carcinogen.

As displayed in Fig. 2.6, some data are available to assess only the oral and dermal carcinogenicity of B[a]A in animals. No information could be located on the effects of B[a]A following inhalation exposure.

2.3.2.3 Summary of relevant ongoing research

Studies of the biological mechanisms of action of PAHs and their molecular dosimetry are being conducted in a number of laboratories. In addition, B[a]A has been listed in the *National Toxicology Program Review of Current DHHS, DOE, and EPA Research Related to Toxicology, Fiscal Year 1986*. (DHHS is the acronym for the Department of Health and Human Services; DOE is the acronym for the Department of Energy.) B[a]A has a toxicology testing status B: on test in February 1986. The chemical is to be tested for mutagenesis/genetic toxicity by the Food and Drug Administration, National Center for Toxicological Research, Division of Genetic Toxicology, and the EPA Office of Research and Development. A comparative-potency method to quantitatively assess the carcinogenic effects for PAHs is under development by the Carcinogen Assessment Group, the Office of Solid Waste, the Office of Drinking Water, and the Office of Air Quality Planning and Standards of the EPA (EPA Contract Number 68-02-4403) and is being applied to the data available for B[a]A.

2.3.3 Other Information Needed for Human Health Assessment

2.3.3.1 Toxicokinetics and mechanisms of action

The metabolism of B[a]A has been examined in several cell cultures, tissue cultures, and microsomal preparations. The metabolism data collected suggest a mechanism of action similar to the one established for benzo[a]pyrene. There is limited information on the toxicokinetics of B[a]A administered via the inhalation route. Similarly, quantitative and mechanistic aspects of the steps leading to elimination of B[a]A are lacking. The information available on B[a]A may be considered insufficient to allow extrapolation from one route of exposure to another. Although it is possible to rely on the toxicokinetics database available for benzo[a]pyrene, it should be considered desirable to generate the requisite information to fill this gap. No current studies were identified as being likely to provide this information.

2.3.3.2 Adequacy of data on biological monitoring

The biological monitoring techniques in which DNA adducts are quantified are limited, because inborn factors, environmental chemistry, and drugs can alter the activity of the enzymes responsible for converting B[a]A to the diol epoxides that bind to DNA. There is a lack of information concerning the use of these techniques in occupationally or environmentally exposed individuals. Additional research needs to include further investigation of the formation of adducts following these exposure situations.

The techniques that use immunoassays to determine the presence of antibodies to PAH-DNA adducts in blood have been tested in occupationally exposed humans and smokers. This technique has reported an association between sera positive for antibodies and occupational exposure and smoking (Harris 1985). The reliability of this method needs to be further examined in other, nonoccupational, exposure situations.

The presence of PAHs or PAH metabolites in urine is an indication that exposure has occurred. However, high environmental concentrations of PAHs in the workplace were not found to be reflected to the same extent in excretion of the PAHs in urine (Becher and Bjorseth 1983, Becher et al. 1984). This problem was suggested to result from the nonbioavailability of particle-bound B[a]A. Therefore, this method may still be applicable in other exposure situations.

In addition, smoking cigarettes and some occupationally related activities result in human exposure to PAHs; therefore, the determination of biological levels of PAHs in smokers and in the general population must be examined more fully to properly assess environmental exposure.

2.3.3.3 Environmental considerations

The accuracy and precision of the analytical methods used to measure ambient B[a]A are somewhat limited; but the current methods, if properly conducted, are sufficient to record ambient levels of B[a]A. However, some methods have limited sensitivity.

Limited data are available to characterize background levels of B[a]A or levels typically found at hazardous waste sites. Comprehensive monitoring studies are being conducted by EPA at or around many hazardous waste sites, but the data are not yet available in a single database.

Limited quantitative data are available on the bioavailability of B[a]A in soil or sorbed onto particulate matter in air. This lack of information limits our understanding of potential health risks in humans following exposure in these media.

Information on the fate of B[a]A sorbed onto particulate matter in air is presently unclear. The role of photochemical oxidation in the removal of B[a]A from air needs to be elucidated. Also, additional information on biodegradation processes and rates in aquatic and terrestrial systems is needed.

Some limited information is available on the interactions of B[a]A with other chemicals in vivo and with other chemicals typically found in the environment and at hazardous waste sites. For example, Bartosek et al. (1984) reported on the in vivo interactions of B[a]A and chrysene administered simultaneously in rats. However, the available information is incomplete; consequently, the risks associated with exposure to B[a]A in the environment are not completely understood.

3. CHEMICAL AND PHYSICAL INFORMATION

3.1 CHEMICAL IDENTITY

The chemical formula, structure, synonyms, and identification numbers for B[a]A are listed in Table 3.1.

3.2 PHYSICAL AND CHEMICAL PROPERTIES

Important physical and chemical properties of B[a]A are given in Table 3.2.

Table 3.1. Chemical identity of benz[a]anthracene

Chemical name: Benz[a]anthracene

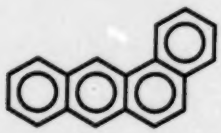
Synonyms: Benzanthracene; 1,2-benz[a]anthracene; 1,2-benzanthracene; benzoanthracene; 1,2-benzoanthracene;benzo[a]anthracene; 2,3-benzophenanthrene; benzo[b]phenanthrene; 2,3-benzaphenanthrene; naphthanthracene; tetraphene; B[a]A; BA (IARC 1983)[a]

Trade name: Not applicable

Chemical formula: $C_{18}H_{12}$ (IARC 1983)

Wiswesser line notation: L D6 B666J (HSDB 1987)

Chemical structure:



Identification numbers:

CAS registry No.: 56-55-3
NIOSH RTECS No.: CV9275000
EPA Hazardous Waste No.: U018
OHM-TADS No.: 800123
DOT/UN/NA/IMCO Shipping No.: Not available
STCC Number: Not available
Hazardous Substances Data Bank No.: 4003
National Cancer Institute No.: Not available

[a]Confusion exists in the literature concerning the naming of this compound, mainly due to the fact that two different systems (Richter and IUPAC) of numbering ring structures have been used; the IARC reference, unfortunately, does not acknowledge that this confusion exists and that some of the synonyms listed are incorrect in nomenclature.

Table 3.2. Physical and chemical properties of benz[a]anthracene

Property	Value	References
Molecular weight	228.29 g/mol	CRC 1987
Color	Colorless	IARC 1983
Physical state	Plates with yellow-blue fluorescence (recrystallized from glacial acetic acid or ethanol)	CRC 1987
Odor	Unknown	
Melting point	162°C	CRC 1987
Boiling point	435°C; sublimes	CRC 1987, Merck Index 1983
Autoignition temperature	Unknown	
Solubility		
Water	Virtually insoluble (9 to 14 μg/L)	IARC 1983
Organic solvents	Slightly soluble in acetic acid and hot ethanol; soluble in acetone and diethyl ether; very soluble in benzene	IARC 1983
Biological fluids	Unknown	
Density	1.274 (20°C)	HSDB 1987
Partition coefficients		
Octanol-water (K_{ow})	4.1×10^5	EPA 1982
Log K_{ow}	5.61	
Soil-organic carbon-water (K_{oc})	2×10^5	EPA 1982
Vapor pressure (20°C)	2.2×10^{-8} mm Hg	EPA 1982
Henry's law constant	1×10^{-6}	EPA 1982
Flash point	Unknown	
Flammability limits	Unknown	
Conversion factor[a]	1 ppm = 9.34 mg/m^3	Verschueren 1983

[a]Calculated using the ideal gas law, $PV = nRT$ at 25°C.

4. TOXICOLOGICAL DATA

4.1 OVERVIEW

B[a]A is absorbed by the oral and dermal routes of exposure; no direct evidence is available for absorption of B[a]A via the lungs. Following oral absorption, B[a]A is distributed to several tissues and accumulates preferentially in the adipose and mammary tissues. It is metabolized to conjugated derivatives and eliminated. It is expected that absorbed B[a]A will be excreted predominantly in the feces, as is true for other PAHs.

B[a]A is metabolized to reactive derivatives that are thought to be responsible for its mutagenic activity in experimental systems. B[a]A is a weak experimental carcinogen by the dermal route of exposure. There is some evidence that it is carcinogenic by the oral route as well. Its carcinogenicity by the inhalation route has not been studied. Mutation is thought to be a necessary (although insufficient) step for the carcinogenic activity of B[a]A.

There is no information on other toxic effects of B[a]A in humans and experimental animals following inhalation, oral, and dermal exposures.

4.2 TOXICOKINETICS

4.2.1 Overview

B[a]A is absorbed by the oral and dermal exposure routes; no direct evidence is available for absorption of B[a]A via the lungs. B[a]A is rapidly absorbed and distributed to several tissues. The relative uptake is dependent on the blood perfusion rate of the tissue. B[a]A accumulates preferentially in adipose and mammary tissues.

B[a]A undergoes metabolic transformations in animals and humans to metabolic intermediates responsible for its toxicity. These metabolic intermediates include arene oxides, dihydrodiols, and diol epoxides. B[a]A 3,4-dihydrodiol and B[a]A 3,4-diol-1,2-epoxide have been shown to have high tumorigenicity on mouse skin and by intraperitoneal (IP) injection into newborn mice (Slaga et al. 1978, Levin et al. 1982).

As is true for other PAHs, absorbed B[a]A is expected to be excreted predominantly in the feces. The excreted material consists largely of B[a]A metabolites, with only a small portion of unchanged hydrocarbon. The excreted products consist of dihydrodiols and phenols either free or conjugated as glucuronide and sulfate esters, and glutathione conjugates. B[a]A metabolites are subject to enterohepatic circulation. The relative rates of elimination are dependent on the

route of administration. Orally administered hydrocarbon is anticipated to exhibit greater elimination rates than that administered by other routes, because of the effect of first-pass metabolism through the liver.

4.2.2 Absorption

4.2.2.1 Inhalation

Human. No quantitative information on the absorption of B[a]A via the respiratory tract was found. Absorption of B[a]A via this route is inferred from identification of B[a]A metabolites in individuals exposed to PAHs in an industrial environment (Becher and Bjorseth 1983).

Animal. No information was found on the absorption of B[a]A via the respiratory tract. In analogy to benzo[a]pyrene, pulmonary absorption of B[a]A is expected to be efficient and to be subject to similar controlling factors. Specifically, the role of metabolism in absorption mechanisms, particle-size matrix effects, and mucociliary clearance are anticipated to influence the rate of absorption via the respiratory tract (Creasia et al. 1976, Tornquist et al. 1985, Medinsky and Kampcik 1985).

4.2.2.2 Oral

Human. No data on the absorption of B[a]A via the gastrointestinal tract in humans were identified.

Animal. The kinetics of oral absorption of B[a]A was studied in the rat (Modica et al. 1983). Absorption was rapid and efficient, with levels in blood, liver, and brain reaching a maximum 1 to 2 h after administration. Qualitative evidence of oral absorption is found in the carcinogenicity studies conducted by gavage administration of B[a]A, as summarized in IARC (1973) and described in Sect. 4.3.5.3.

4.2.2.3 Dermal

Human. No data on the dermal absorption of B[a]A in humans were identified. The rate of dermal penetration of B[a]A is not likely to be significantly different from that of benzo[a]pyrene. For the latter, under in vitro conditions, 3% of an applied dose of [^{14}C]benzo[a]pyrene (10 $\mu g/cm^2$) permeated human skin in 24 h (Kao et al. 1985).

Animal. The relative rate of dermal penetration of B[a]A painted on the skin of mice was determined to be similar to that of benzo[a]pyrene (Bock and Burnham 1960). The concentrations in the skin, as detected by fluorometry, reached a maximum 2 h after topical application of a 1% solution of the hydrocarbons. The permeation rate for benzo[a]pyrene in the mouse for a 24-h exposure has been reported as 10% (Kao et al. 1985) and 40% (Sanders et al. 1986) of an applied dose of 10 $\mu g/cm^2$ and 1.25 to 125 $\mu g/cm^2$ of [^{14}C]benzo[a]pyrene, respectively. Evidence of dermal absorption in animals is found in the carcinogenicity studies summarized in IARC (1973).

4.2.3 Distribution

There is no quantitative information on the distribution of either inhaled or dermally absorbed B[a]A.

Orally absorbed B[a]A is rapidly and widely distributed among several tissues (Modica et al. 1983). Maximum concentration in perfused tissues (liver, blood, and brain) was reached in 1 to 2 h, while slowly perfused tissues (mammary and adipose) reached peak levels in 3 to 4 h. Bartosek et al. (1984) determined the relative tissue affinity for B[a]A in young rats, 72 h after oral administration of 22.8 mg or 11.4 mg, to be: adipose > mammary > brain > liver > blood.

4.2.4 Metabolism

The metabolism of B[a]A in human and animal systems apparently proceeds via the biotransformation pathways established for benzo[a]pyrene [Cooper et al. 1983, Levin et al. 1982, Sims 1982, Thakker et al. 1982 (see Fig. 4.1)].

Briefly, the primary transformations are oxidation of the aromatic nucleus to form arene oxides and hydrolysis of these epoxide intermediates to *trans*-dihydrodiols in a reaction catalyzed by epoxide hydrolase (Sims and Grover 1974). The dihydrodiols formed during the metabolism of B[a]A are the 1,2-, 3,4-, 10,11-, 5,6-, and 8,9-diol. The last two are major diol metabolites of B[a]A.

Secondary metabolism involves conjugation of arene oxides with glutathione catalyzed by the glutathione transferases (Keysell et al. 1975); formation of sulfate and glucuronide conjugates of phenols (from nonenzymatic rearrangement of arene oxides) and *trans*-dihydrodiols (Sims and Grover 1981); and oxidation of benzo-ring *trans*-dihydrodiols to diol epoxides (Sims 1982). The diol epoxides derived from the 3,4-diol and 8,9-diol have been shown to be important intermediates in the metabolism of B[a]A. The diol epoxide derived from the B[a]A 3,4-diol has been shown to be a potent mutagen (Wood et al. 1977a,b). Tumorigenicity of the diol epoxide was shown by Levin et al. (1978) and Wislocki et al. (1978).

The stereochemistry of the oxidative steps leading to epoxide and diol metabolites of B[a]A has been elucidated (Thakker et al. 1982, Mushtaq et al. 1985).

4.2.5 Excretion

The steps involved in the excretion of B[a]A are likely to be those established for other PAHs. Metabolism, hepatobiliary excretion, and elimination through feces are the dominant features in the process that has been delineated for other PAHs (Boyland and Sims 1964; Schlede et al. 1970a,b). The material excreted is expected to consist predominantly of dihydrodiol and phenol conjugates (glucuronide and sulfate esters) and glutathione conjugates.

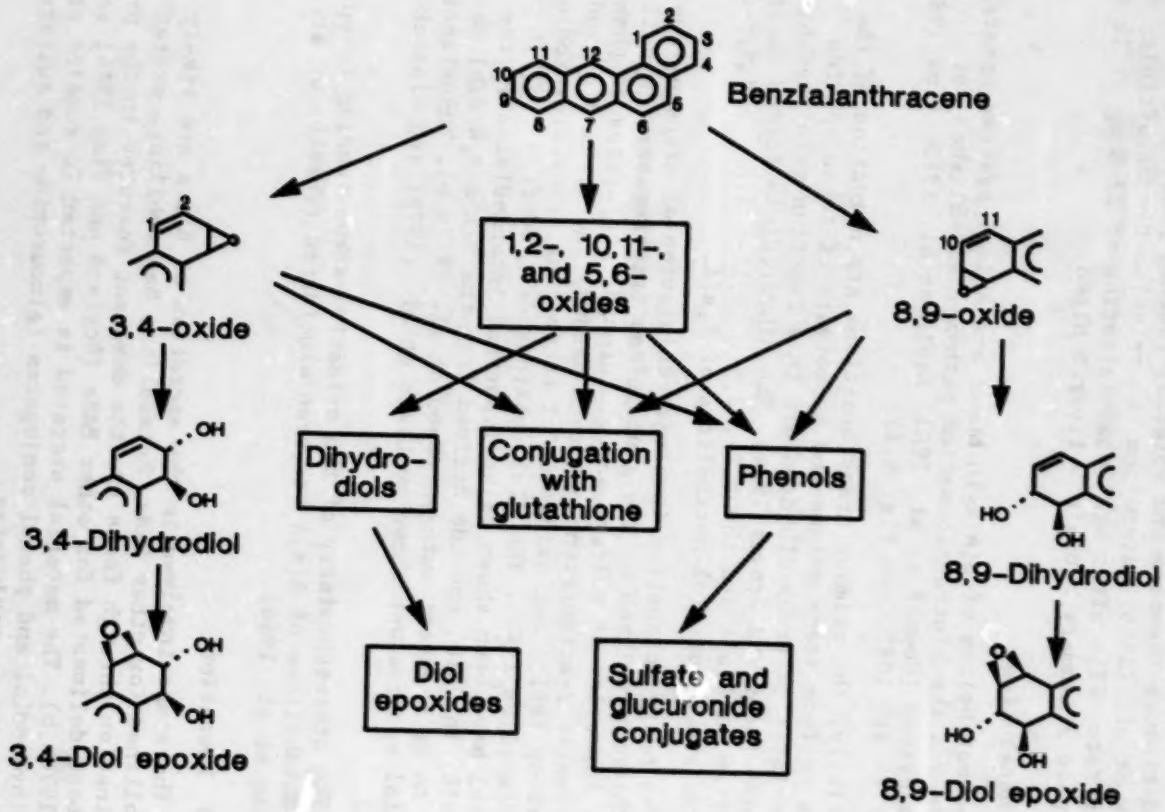


Fig. 4.1. Metabolic fate of benz[a]anthracene.

4.3 TOXICITY

4.3.1 Lethality and Decreased Longevity

Pertinent data regarding lethality and decreased longevity in humans or experimental animals following inhalation, oral, or dermal exposure to B[a]A could not be located in the available literature.

4.3.2 Systemic/Target Organ Toxicity

No information is available on the systemic effects of B[a]A in humans or experimental animals following inhalation, oral, or dermal exposures. The carcinogenic PAHs as a group cause skin disorders and have an immunosuppressive effect; however, specific health effects caused by exposure to B[a]A have not been reported.

In a number of older investigations, topical application of B[a]A has been reported to suppress the sebaceous glands in mouse skin (Bock and Mund 1958). Bock and Mund (1958) applied 0.2 mL of B[a]A, twice daily, to two-thirds of the shaved backs of Swiss mice. Four days after the last application, mice were sacrificed. The treated skin was then subjected to an elaborate preparation and staining procedure and was qualitatively examined. B[a]A was reported to suppress sebaceous glands. However, controls were not employed, and therefore it is not possible to determine whether the effects seen were due to the solvent and/or the preparation procedures.

4.3.3 Reproductive and Developmental Toxicity

Pertinent data regarding the reproductive and developmental toxicity of B[a]A in humans or experimental animals following inhalation, oral, or dermal exposure could not be located in the available literature.

4.3.4 Genotoxicity

4.3.4.1 Overview

The genetic toxicity of B[a]A has been evaluated experimentally in a variety of short-term genetic toxicology assays utilizing prokaryotes and eukaryotes as target or indicator organisms for potential genotoxic effects. The metabolism of B[a]A is an essential event in producing genotoxic effects in both in vitro and in vivo biological test systems. The test systems used to evaluate the genotoxicity of B[a]A and the reported results are summarized in Tables 4.1 and 4.2.

B[a]A undergoes metabolism to form several intermediates. Studies have indicated that the 3,4-dihydrodiol metabolite may represent the proximate and the 3,4-diol-1,2-epoxide metabolite may represent the ultimate carcinogenic and mutagenic forms of B[a]A (Slaga et al. 1978; Wood et al. 1976, 1977a,b). These reactive electrophilic intermediates are capable of interacting and binding to DNA to form bulky DNA adducts, which are generally regarded as an important determinant in mutagenesis and in clastogenesis (Brendel and Ruhland 1984, Fahl et al. 1981). The

Table 4.1. Genetic toxicity of benz[a]anthracene (in vitro)

End points	Species (test systems)	Results w or w/o activation[a]	References
DNA damage	*Escherichia coli* (pol A−/pol A+)	Negative w activation	Rosenkranz and Poirier 1979
DNA damage (UDS)	Primary rat hepatocytes	Negative w/o activation	Williams 1977
	Primary rat hepatocytes	Positive w/o activation	Probst et al. 1981, Tong et al. 1981a
	Rat tracheal epithelial cells	Negative w/o activation	Ide et al. 1981
	HeLa cells	Positive w activation	Martin et al. 1978
	Human fibroblasts	Negative w/o activation	Stich and San 1973, San and Stich 1975
Mitotic recombination	*Saccharomyces cerevisiae* D3	Negative w activation	Simmon 1979a
Gene mutations	*Salmonella typhimurium* (his+/his−):TA98, TA100, TA1538	Positive w activation	Coombe et al. 1976, Conney 1982, McCann et al. 1975, Simmon 1979b, Bartsch et al. 1980, Dunkel et al. 1984
	Salmonella typhimurium (his+/his−):TA1535, TA1538	Negative w activation	Rosenkranz and Poirier 1979
	Salmonella typhimurium (his+/his−):TA1538	Positive w activation (host-mediated activation)	Simmon et al. 1979, Poirier and de Serres 1979
	Salmonella typhimurium (8AGs/8AGr):TM677	Positive w activation	Kaden et al. 1979
	Escherichia coli WP2 uvrA	Negative w activation	Dunkel et al. 1984
	V79/HGPRT (6-TG)	Positive w activation	Kraha and Heidelberger 1977
	V79/APRT (8-AG)	Negative w activation	Huberman and Sachs 1974, 1976; Huberman 1975
	V79/APRT (8-AG)	Negative w/o activation	Marquardt et al. 1979
	V79/Na+,K+ ATPase (Ouabain)	Positive w activation	Slaga et al. 1978
	Mouse lymphoma L5178Y cells/TK +/−	Positive w activation (S9 mix)	Amacher et al. 1980, Amacher and Turner 1980, Clive et al. 1979
	Mouse lymphoma L5178Y cells/TK +/−	Negative w activation (rat hepatocytes)	Amacher and Paillet 1983
	ARL/HGPRT	Negative w/o activation	Tong et al. 1981b, Ved Brat et al. 1983

Table 4.1 (continued)

End points	Species (test systems)	Results w or w/o activation[a]	References
Gene mutations (continued)	Human EUE epithelial-like cells (diptheria toxin)	Negative w/o activation	Rocchi et al. 1980
	Human keratinocytes (HGPRT)	Negative w activation	Allen-Hoffman and Rheinwald 1984
Sister chromatid exchange (SCE)	CHO	Positive w/o activation	Pal 1981
	ARL	Positive w/o activation	Tong et al. 1981a
Chromosomal aberrations	V-79	Positive w/o activation	Kochlar 1982
	Syrian hamster cells	Negative w/o activation	Benedict et al. 1972
Cellular transformation	Syrian hamster embryo cells (clonal assay)	Positive w/o activation	Benedict et al. 1972; DiPaolo et al. 1969, 1971; Pienta et al. 1977
	Syrian hamster embryo cells (clonal assay)	Negative w/o activation	Huberman et al. 1972
	Mouse prostate C3HG23 cells	Positive w activation	Marquardt and Heidelberger 1972
	Mouse C3H/10T1/2 embryo fibroblasts	Negative w/o activation	Nesnow and Heidelberger 1976
	Mouse C3H-M2 fibroblasts	Positive w/o activation	Marquardt et al. 1979
	RLV/Fischer rat embryo cells	Positive w/o activation	Dunkel et al. 1981, Freeman et al. 1973
	Mouse BALB/C3T3 cells	Positive w/o activation	Dunkel et al. 1981

[a]The results presented in Tables 4.1 and 4.2 are based on the activity profiles prepared by Waters et al. (1987), Gene-Tox data files supplied by John S. Wassom, and/or personal review of the original citation.

Table 4.2. Genetic toxicity of benz[a]anthracene (in vivo)

End points	Species (test systems)	Results[a]	References
Chromosomal aberrations	Chinese hamster bone marrow cells	Positive	Basler and Rohrborn 1978
	Chinese hamster bone marrow cells	Negative	Roszinsky-Kocher et al. 1979
	Long-Evans rat bone marrow cells	Negative	Sugiyama 1973
	Chinese hamster bone marrow erythrocytes (micronuclei)	Positive	Peter et al. 1979
	NMRI mice metaphase II oocytes	Positive	Peter et al. 1979
	Chinese hamster spermatogonia	Positive	Basler and Rohrborn 1978
Sister chromatid exchange	Chinese hamster bone marrow cells	Positive	Roszinsky-Kocher et al. 1979
Gene mutations	*Drosophila melanogaster* (somatic mutation)	Negative	Fahmy and Fahmy 1980
	Drosophila melanogaster (sex-linked recessive lethal)	Negative	Fahmy and Fahmy 1973, Zijlstra and Vogel 1984

[a]The results presented in Tables 4.1 and 4.2 are based on the activity profiles prepared by Waters et al. (1987), Gene-Tox data files supplied by John S. Wassom, and/or personal review of the original citation.

genotoxicity of B[a]A is dependent on metabolic activation, either exogenously supplied or endogenously present, and the predominance or ratio of activation and detoxification pathways.

4.3.4.2 General discussion

The genotoxicity of B[a]A has been demonstrated in various in vivo and in vitro genetic toxicology assays. The majority of the experimental results reported have been positive, but there are negative results as well.

B[a]A has been tested for in vivo heritable genetic effects, but only in *Drosophila melanogaster*. The results were negative for sex-linked recessive lethal mutation and somatic mutation via oral and injection routes of administration (Fahmy and Fahmy 1973, 1980; Zijlstra and Vogel 1984). Generally, B[a]A showed positive genotoxic responses for other genetic end points when tested in vivo. Increased chromosomal aberrations were reported for B[a]A in Chinese hamster bone marrow cells and spermatogonia and in mouse oocytes (Basler and Rohrborn 1978, Peter et al. 1979). Also, positive results were reported for the in vivo hamster micronuclei assay (Peter et al. 1979). The positive results reported for rodent germ cells (Peter et al. 1979, Basler and Rohrborn 1978) may indicate a potential for heritable genetic damage. A weak induction of sister chromatid exchange in Chinese hamster bone marrow cells was observed as well (Roszinsky-Kocher et al. 1979).

Both positive and negative results have been reported in in vitro test systems. Positive results were reported in the host-mediated gene mutation assay with *Salmonella typhimurium* strain TA1538 (Simmon et al. 1979, Poirier and de Serres 1979). Negative results were reported for the microsomal-mediated Ames assay using strains TA1535 and TA1538 (Rosenkranz and Poirier 1979). However, B[a]A induced positive mutagenic responses in bacterial assays with *Salmonella typhimurium* strain TA100 (Conney 1982, Coombs et al. 1976, McCann et al. 1975, Simmon 1979b), strain TM677 (Kaden et al. 1979), and other bacterial strains (Dunkel et al. 1984). Results were negative for DNA damage in *Escherichia coli* (Rosenkranz and Poirier 1979) and mutations in *Saccharomyces cerevisiae* D3 (Simmon 1979a). However, positive results were reported in the majority of mammalian cell systems (see Table 4.1).

There is sufficient evidence from short-term in vivo and in vitro assays to indicate that B[a]A is a genotoxic agent when metabolically activated to the diol and diol-epoxide forms. Discrepancies in the reported results may be attributed to shortcomings associated with the use of metabolic activation systems and the delicate balance of existing enzymatic pathways. Recently, the sensitivities of some in vitro assays have improved by refinement of procedures in performing these assays. B[a]A is present as a component of the total content of PAHs in the environment. Interactions among various PAHs present in complex environmental mixtures and their effects on the potential of B[a]A for human genotoxicity are uncertain. It is reasonable to assume that human exposure to genotoxic components of PAH mixtures such as B[a]A will present a risk to humans by inducing heritable genetic damage and potential human carcinogenesis.

4.3.5 Carcinogenicity

4.3.5.1 Overview

The carcinogenicity of B[a]A has not been well studied. There are no reports directly correlating human B[a]A exposure and tumor development, although humans are likely to be exposed by all routes; however, there are a number of reports associating human cancer with exposure to mixtures of PAHs that include B[a]A. There is experimental evidence that B[a]A is a skin carcinogen in animals following dermal application, and there is some evidence of carcinogenicity by the oral route. It is possible that B[a]A could cause cancer in humans as well.

4.3.5.2 Inhalation

Human. No studies on the carcinogenicity of B[a]A in humans following inhalation exposure were found in the available literature. However, epidemiologic studies have shown an increased incidence of lung cancer in humans exposed to coke oven emissions (Lloyd 1971, Redmond et al. 1972, Mazumdar et al. 1975), roofing tar emissions (Hammond et al. 1976), and cigarette smoke (Wynder and Hoffmann 1967, Maclure and MacMahon 1980, Schottenfeld and Fraumeni 1982). Each of these mixtures contains B[a]A as well as other carcinogenic PAHs and other potentially carcinogenic chemicals such as nitrosamines. It is thus impossible to evaluate the contribution of B[a]A to the total human carcinogenicity of these mixtures, because of their complexity and the presence of other carcinogens. Reports of this nature provide a qualitative suggestion of the potential for B[a]A-induced carcinogenicity, nonetheless.

Animal. No studies on the carcinogenicity of B[a]A in animals following inhalation exposure were found in the available literature.

4.3.5.3 Oral

Human. No studies on the carcinogenicity of B[a]A in humans following oral exposure were found in the available literature.

Animal. No studies concerning the carcinogenicity of B[a]A in animals following oral exposure via the diet or drinking water were available; however, two studies were located in which B[a]A was administered by gavage. In these studies, mice received intermittent doses of B[a]A for 5 weeks (Klein 1963) or for unspecified intermediate lengths of time (Bock and King 1959); the protocols and results are summarized in Table 4.3. Although significantly elevated incidences of hepatomas and lung adenomas were observed (Klein 1963), neither of these studies was adequately reported; they did not include complete histopathology, adequate treatment or study durations, or large enough sample sizes. In addition, the authors did not determine whether B[a]A produced malignant tumors. As a result, the studies were judged inadequate to support the development of significant human exposure levels for carcinogenicity for the purposes of this document, although they do provide some evidence for the potential carcinogenicity of B[a]A by the oral route.

Table 4.3. Tumorigenic effects of benz[a]anthracene following administration by gavage

Source	Species	Dose	Treatment duration	Study duration	Target organ	Tumor type	Tumor incidence[a] (%)
Klein 1963	Male B6AF1/J mice	0 (vehicle)[b]	5 weeks, 3 doses/week	444 to 547 days	Lung	Adenoma	17/58 (29)
					Liver	Hepatoma	2/58 (3)
		1.5 mg	5 weeks, 3 doses/week	437 to 547 days	Lung	Adenoma	56/59 (95)
					Liver	Hepatoma	38/59 (64)
Bock and King 1959	C57BL mice (sex not specified)	0 (vehicle)[c]	Single dose	16 months	Forestomach	Papilloma	0/12 (0)
		0.5 mg	Single dose	16 months	Forestomach	Papilloma	0/13 (0)
		0 (vehicle)[c]	8 doses at 3- to 7-day intervals	16 months	Forestomach	Papilloma	0/16 (0)
		4.0 mg	8 doses at 3- to 7-day intervals	16 months	Forestomach	Papilloma	1/19 (5)
		0 (vehicle)[c]	16 doses at 3- to 7-day intervals	16 months	Forestomach	Papilloma	0/6 (0)
		8.0 mg	16 doses at 3- to 7-day intervals	16 months	Forestomach	Papilloma	1/8 (12)

[a]Numbers in parentheses are percentages.
[b]Vehicle = dioctyl ester of sodium sulfo-succinic acid.
[c]Vehicle = mineral oil.

4.3.5.4 Dermal

Human. No studies on the carcinogenicity of B[a]A in humans following dermal exposure were found in the available literature. As with inhalation exposure, however, there are reports of skin cancer among individuals exposed dermally to mixtures of PAHs containing B[a]A. The earliest of these is the report of Pott (1775) of scrotal cancer among chimney sweeps. More recently, skin cancer among those exposed dermally to shale oils has been reported (Purde and Etlin 1980). These reports provide only qualitative suggestion of the human carcinogenic potential of B[a]A, however, due to the presence of other putative carcinogens in the mixtures.

Animal. B[a]A has been shown to cause skin tumors in mice following dermal application. The results of a key study by Bingham and Falk (1969) are shown in Table 4.4. In this experiment, graded concentrations of B[a]A in toluene or *n*-dodecane were applied topically to the backs of C3H/He mice (sex unspecified) three times a week for 50 weeks, and local tumors were quantitated. Dose-related increases in tumor incidence were observed. The method of application was not specified, and no solvent controls were included, however. This experiment demonstrated an enhanced skin tumor incidence when B[a]A was administered in *n*-dodecane as compared with toluene. Inadequate mechanistic data are available to evaluate the nature of the observed cocarcinogenic activity.

Despite the limitations of this study, a dose-response relationship for the carcinogenicity of B[a]A was demonstrated. The dose-response is extremely shallow (sublinear) over a 2 order-of-magnitude dose range. One explanation for this response could be that the administered dose and the biologically active dose at the target site (reactive form of the agent at the site of action) are not directly proportional at the high doses employed (due to mechanisms of interaction such as saturation of metabolic activating systems). Tumors were observed at dose levels of about 0.34 mg/kg (0.15 mg/kg/day) and above but were not seen at 0.034 mg/kg (0.015 mg/kg/day). By comparison, the more potent carcinogen benzo[a]pyrene caused tumors in mice in a similar experiment at doses as low as 0.014 mg/kg/day (Habs et al. 1980).

4.3.5.5 General discussion

The only end point of toxicity that has been adequately evaluated for B[a]A is that of dermal carcinogenicity, although there is some evidence for oral carcinogenicity as well. B[a]A has also been shown to elicit tumors by subcutaneous injection in mice (IARC 1973). The mechanism of B[a]A-induced carcinogenicity is likely to be similar to that of other PAHs; namely, involving metabolic activation to reactive diol epoxide derivatives that can form adducts with DNA which lead to mutation and tumor initiation under certain circumstances (IARC 1983).

4.4 INTERACTIONS WITH OTHER CHEMICALS

Most human exposures to B[a]A are not to the pure compound but to particle-bound B[a]A; the presence of particles is likely to affect its pharmacokinetics and carcinogenicity. Sun et al. (1982) showed that when the carcinogenic polycyclic aromatic hydrocarbon benzo[a]pyrene

Table 4.4. Carcinogenic activity of benz[a]anthracene on mouse skin

Vehicle	Dose		Tumor incidence[a]			
	Percent concentration[b]	mg/kg/day[c]	Malignant		Benign	
Toluene	1.0	7.5	5/29	(17)	3/29	(10)
Toluene	0.2	1.5	3/32	(9)	0	
Toluene	0.02	0.15	1/18	(6)	0	
Toluene	0.002	0.015	0/32	(0)	0	
n-Dodecane	1.0	7.5	16/22	(73)	1/22	(5)
n-Dodecane	0.2	1.5	7/21	(33)	4/21	(19)
n-Dodecane	0.02	0.15	4/20	(20)	0/20	(20)
n-Dodecane	0.002	0.015	4/21	(19)	4/21	(19)
n-Dodecane	0.0002	0.0015	2/31	(6)	2/31	(6)

[a]Numbers in parentheses are percentages.

[b]50 mg by weight of the solution was administered at each dosing. Animals were treated three times weekly for 50 weeks.

[c]This conversion was made by assuming that a mouse weighs 0.035 kg and that the density of the dosing solution is equal to that of toluene itself (0.87).

Source: Bingham and Falk 1969.

was particle-bound, it was cleared from hamster lungs much more slowly than a pure B[a]P aerosol, thus increasing the length of time the lungs were exposed, and also increasing the dose to the gastrointestinal tract as a result of mucociliary clearance. Respirable PAH-containing particulates such as diesel exhaust, when coated with the phospholipid component of a pulmonary surfactant, are genotoxic (Wallace et al. 1987). Dusts can increase the rates of pulmonary cell proliferation (Harris et al. 1971, Stenback et al. 1976, Stenback and Rowland 1979), which in turn increases the susceptibility of those cells to an initiation event in the presence of a carcinogen. Coadministration of B[a]P and particles greatly increases respiratory tract tumor yields in experimental animals (Stenback et al. 1976, Stenback and Rowland 1979). The effects of particles on potential B[a]A carcinogenesis is likely to be similar.

Human exposure to B[a]A in the environment occurs seldom, if ever, to B[a]A alone but to B[a]A as a component of complex mixtures of PAHs and other chemicals. Interactions between B[a]A and other mixture components are likely to occur. In particular, interactions may play a large part in carcinogenesis resulting from experimental exposure to PAHs. For example, Mahlum et al. (1984) have shown that different temperature-range distillates of coal liquids have different skin-tumor-initiating activities in mice, despite the fact that they contain similar levels of known carcinogenic PAHs. This difference is believed to be due to the modifying effects of the spectrum of noncarcinogenic PAHs obtained at different temperatures. Most of the PAH components of coal liquid fractions obtained at different temperatures will vary both qualitatively and quantitatively, and consequently their abilities to modify carcinogenesis will vary accordingly. The relative roles of the PAH components of each of such mixtures is unknown, however, so that quantitative evaluation is not possible. Since human exposure occurs to mixtures of PAHs, and not individual components, quantitative evaluation of the toxicity of individual PAHs is probably insufficient.

Human exposure to complex mixtures of PAHs has been extensive; and some adverse effects are well-documented, particularly carcinogenic effects following long-term exposure. The extent of human exposures to well-defined PAH mixtures that are responsible for producing excess disease is generally not known in quantitative terms. Coke oven emissions and related substances such as coal tar have probably been the most widely studied. Coal tar derivatives were most likely responsible for the first observation of occupational cancer, that of scrotal cancer among London chimney sweeps, made by Pott (1775). More recent mortality studies have demonstrated strong associations between human exposure to coke oven emissions and excess disease; specifically, significant increases in lung and genitourinary cancer mortality have been observed (IARC 1983). The earliest of these reports was made in 1936 by investigators in Japan and England (Kennaway and Kennaway 1936) who were studying lung cancer mortality among persons employed in coal carbonization and gasification processes. Subsequent studies conducted in the United States clearly demonstrated substantial increases in lung and genitourinary system cancer mortality among coke oven workers (Lloyd 1971, Redmond et al. 1972, IARC 1984). Human tumorigenicity has also been reported to result from exposure to creosote. Creosote is a generic

term that refers to wood preservatives derived from coal tar, creosote, or coal tar neutral oil, and includes extremely complex mixtures of liquid and solid aromatic hydrocarbons. Workers who engaged in activities such as dipping timbers in creosote were reported to have developed malignant and premalignant skin lesions of the face, arms, and scrotum (O'Donovan 1920, Cookson 1924, Henry 1947, Lenson 1956). Many of the individual PAH components of creosote, such as B[a]A, have been shown to be both mutagenic and carcinogenic in laboratory bioassays, supporting the evidence of its human carcinogenicity (IARC 1983).

Exposures to many other complex chemical mixtures that include PAHs, such as the use of tobacco products and exposure to roofing tar emissions and shale oils, have been associated with human disease incidence. Although this discussion falls short of providing a thorough review of the extensive literature available on the experimental and epidemiological observations of the toxicity of PAH mixtures, its purpose has been to provide examples wherein such toxicity has been documented, in order to emphasize that human exposure occurs to multiple PAHs.

Predicting the toxicity of a complex mixture on the basis of one or several of its components may be misleading because of the possibility of interactions among the components that may modify toxicity. For example, both carcinogenic and noncarcinogenic PAHs may compete for the same metabolic activating enzymes and thereby reduce the toxicity of carcinogenic PAHs. Exposure to other PAHs may induce enzyme levels leading to more rapid detoxication of B[a]A, reducing its carcinogenicity (Slaga and diGiovanni 1984, Weibel 1980). Naturally occurring compounds have been found to induce the enzymes that metabolize PAHs, leading to either increased or decreased toxicity. For example, plant flavonoids can induce microsomal monooxygenases and reduce the carcinogenicity of B[a]A (Weibel 1980). Environmental contaminants such as TCDD can also increase microsomal enzyme activity and consequently affect PAH toxicity (Kouri et al. 1978). Interactions can thus play important modulating roles in PAH toxicity that may not be adequately reflected in the identification of significant human exposure levels based on the toxicity of single PAHs, since human exposure occurs to mixtures of PAHs.

5. MANUFACTURE, IMPORT, USE, AND DISPOSAL

5.1 OVERVIEW

B[a]A is in the Toxic Substances Control Act (TSCA) Chemical Inventory (EPA 1979a), which lists chemicals (as defined by TSCA) that have been manufactured, imported, or processed for a commercial purpose in the United States since January 1, 1975. B[a]A also occurs in fossil fuels and as a result of the incomplete combustion of fuel and wood. B[a]A is available as a research chemical from some specialty chemical firms. B[a]A and other PAHs are found in coal tar and in the creosote oils and pitches formed from the distillation of coal tars. Coal tar pitch is primarily used as a binder for electrodes. Creosote is primarily used as a wood preservative. Coal tar is also used as a therapeutic treatment for skin diseases such as psoriasis. PAHs are also found in limited amounts in bitumens and asphalt.

5.2 PRODUCTION

The primary source of B[a]A in air is incomplete combustion of wood and fuel for residential heating (EPA 1985). Crude coal tar is produced as a by-product in the formation of coke from coal. Hot gases and vapors that are released from the conversion of coal to coke are collected in a scrubber, which condenses these gases into ammonia, water, crude tar, and other by-products. A typical coke oven produces 80% coke, 12% coke-oven gas, 3% coal tar, and 1% crude benzene. The coal tar is then distilled to yield a number of chemical oils, creosote, and coal tar pitch. The coal tar pitch residue is 40.5% of the crude tar; creosote is approximately 11.5%. Heavy and light creosote also make up a small percentage of distillate (NIOSH 1977). Coal tar contains approximately ~0.007 mg/kg B[a]A; coal tar pitch contains <10 mg/kg B[a]A; and creosote oil contains <3 mg/kg B[a]A (EPA 1985).

As of 1981, the world output of crude coal tar was 1.8×10^7 metric tons; 1.4×10^7 metric tons was of coke-oven origin. In 1980, the U.S. production of crude tar was 2.4×10^6 metric tons. Creosote oil production in the United States in 1981 was estimated to be 5.1×10^5 metric tons. The coal tar pitch production in the United States in 1974 was estimated to be 1×10^6 metric tons (McNeil 1983).

Bitumens and asphalt (a mixture of bitumen with mineral materials) are derived from crude oil. Bitumen samples have been reported to contain 0.15 to 35 mg/kg B[a]A (IARC 1985).

5.3 IMPORT

In 1985, the United States imported a total of almost 12×10^6 gal of creosote oil from the Netherlands, France, West Germany, and other countries and almost 185×10^6 lb of coal tar pitch, blast furnace tar,

and oil-gas tar from Canada, Mexico, West Germany, Asian countries, Australia, and other countries (USDOC 1986).

5.4 USE

B[a]A has some use as a research chemical. It is available from some specialty chemical firms in quantities of 1 to 5 g (Aldrich Chemical Co. 1986).

Coal tar pitch is removed from the tar still as a residue. The rate of feeding and firing of the still regulates the viscosity of the tar. Coal tar pitch is primarily used as a binder for electrodes in the aluminum reduction process; it is used to bind the carbon electrodes used in the reduction pots (NIOSH 1977). In North America, coal tar pitch is also used as the adhesive in membrane roofs (McNeil 1983).

Almost 99% of the creosote produced is sold to wood preservation plants; 0.1 to 0.2% is sold to individual customers (NIOSH 1977). Creosote is used in the preservation of railroad ties, marine pilings, and telephone and telegraph poles. Some creosote is also consumed as fuel by steel producers (NIOSH 1977).

Coal tar is also used in the clinical treatment of skin disorders such as eczema, dermatitis, and psoriasis. The use of dermatological coal tar preparations is extensive (NIOSH 1977).

5.5 DISPOSAL

Following small input of B[a]A from coal-tar creosote, 0.85 mg/L B[a]A has been found in water raw discharge from timber product industries in 1978 (EPA 1985).

Total B[a]A wastewater discharge in 1978 from coke-making operations was reported as 7 metric tons (EPA 1985).

6. ENVIRONMENTAL FATE

6.1 OVERVIEW

B[a]A in the environment is derived from both natural (e.g., wildfires, volcanoes) and man-made sources, but B[a]A originating from man-made sources is, quantitatively, the most significant. B[a]A is formed during high-temperature pyrolytic processes; consequently, natural and man-induced combustion are the major sources of environmental B[a]A. Virtually all direct releases of B[a]A into the environment are to the air. Small and approximately equal amounts are released to water and land. B[a]A is removed from the atmosphere by photochemical oxidation and dry or wet deposition to land or water. B[a]A that reaches the surface will likely remain and will be partitioned primarily to soil/sediment, where it is very persistent. The major degradation process for B[a]A in soil/sediment is biodegradation. Biodegradation is a slow process; a half-life of over 400 days has been reported for B[a]A in soil.

6.2 RELEASES TO THE ENVIRONMENT

Incomplete combustion of carbonaceous material is the major source of B[a]A in the environment. Residential heating and open burning (man-induced and natural) are the largest combustion sources. The large quantity of B[a]A released by these sources is primarily a consequence of inefficient combustion processes and uncontrolled emissions. Of all home heating sources, wood heating is the greatest contributor to B[a]A emissions. In a recent assessment of B[a]A sources and release volumes across the United States, EPA (1985) estimated that home wood combustion contributed 122 metric tons, or 34% of all released volumes. Open burning sources, overall, are responsible for 200 metric tons, or 56% of total B[a]A releases. Prescribed burning is responsible for 100 metric tons of that total, wildfire is responsible for 60 metric tons, and agricultural burning is responsible for 40 metric tons. All other sources (e.g., coal tar, creosote, asphalt, and bitumen production and use) individually contribute 2% or less to total B[a]A releases.

Of all estimated environmental releases of B[a]A, 94% are to air. Of the remaining 6%, approximately equal amounts of B[a]A are released to water and land.

Although they are the source of small amounts of B[a]A and other PAHs on a national scale, hazardous waste sites can be concentrated sources of PAHs on a local scale. For example, abandoned wood treatment plants are sources of high concentrations of creosote, and former manufactured-gas plants (town gas sites) are sources of high concentrations of coal tar. Both creosote and coal tar are composed of a

variety of PAHs, including B[a]A. PAHs at these sites are likely to occur in the soil and on suspended particulate matter in the air.

6.3 ENVIRONMENTAL FATE

The environmental fate of B[a]A is determined, to a large degree, by the chemical's low water solubility and high propensity for binding to particulate or organic matter. As a result, B[a]A in the atmosphere is associated almost exclusively with particulate matter, especially soot, whereas the majority of B[a]A in aquatic systems is strongly bound to suspended particles or bed sediments. Likewise, B[a]A is strongly sorbed to surface soils. Dispersion of particle-bound B[a]A is the primary transport process within air, water, and land.

Based upon an analogy to benzo[a]pyrene, dry deposition of particle-bound B[a]A is probably the most significant transport process between air and land or water (EPA 1979b), although wet deposition is known to occur (DenHollander et al. 1986). Because of a very low vapor pressure, B[a]A that reaches the surface will likely remain and will be partitioned primarily to soil/sediment. Sediment/particle adsorption or biotic uptake are the primary transport processes for the removal of waterborne B[a]A. Desorption into water from soil is very unlikely, and erosion of contaminated soils by surficial runoff is the most probable process for transport of soil-bound B[a]A to aquatic systems.

Information about the fate of particulate PAHs, including B[a]A, released to the atmosphere is presently unclear. It is generally assumed, however, that photochemical oxidation processes play an important role. Atmospheric half-lives of the order of days have been suggested (NAS 1972). PAHs strongly absorb solar radiation at wavelengths above 300 nm, and there is sufficient evidence to indicate that PAHs undergo photooxidation in solution, as pure solids, and when adsorbed onto certain solid substrates such as alumina (NAS 1972). Singlet oxygen has been implicated as the primary oxidant; and endoperoxides and, ultimately, quinones have been implicated as the reaction products (NAS 1972).

It has been inferred that similar processes take place when the compounds are adsorbed on airborne particles. Kamens et al. (1986) reported that B[a]A and other PAHs adsorbed on soot particles rapidly decayed in the presence of sunlight. However, photooxidation of these same compounds adsorbed on carbon black particles was extremely slow (Barofsky and Baum 1976). Similarly, Korfmacher et al. (1980a,b) found that benzo[a]pyrene and other PAHs that are adsorbed on fly ash are highly resistant to photodegradation. More research is needed to elucidate the fate and substrate dependency of atmospheric B[a]A degradation.

Within aquatic systems, B[a]A accumulates in the sediment and is transported with suspended sediment. PAHs, such as B[a]A, in the water column also accumulate in aquatic organisms. However, many organisms metabolize and excrete PAHs rapidly, so that bioaccumulation is a short-term process. For example, in bluegill sunfish, an 89% loss of benzo[a]pyrene was recorded 4 h after exposure (Leversee et al. 1981). Lee et al. (1972) reported rapid elimination of benzo[a]pyrene in three species of California marine teleosts. Depuration rates in invertebrate

species vary more widely. Some species, such as hard-shell clams, show little or no depuration, while others, such as many oysters, eliminate virtually all PAHs following exposure (Eisler 1987).

Aquatic organisms also can assimilate PAHs from food. For example, crustaceans and fish have been reported to readily assimilate PAHs from contaminated food (Eisler 1987). However, in many cases where assimilation of PAHs has been demonstrated, metabolism and excretion of PAHs were rapid (Eisler 1987). In laboratory aquatic ecosystem studies in which radiolabeled B[a]P was used, Lu et al. (1977) found that B[a]P can be accumulated through the food to high levels in the mosquito fish. After 3 days of exposure, the intact parent compound comprised over 50% of the extractable radiolabeled carbon in fish. However, after 33 days of exposure, the intact parent compound comprised only 7% of the total extractable radiolabeled carbon, indicating extensive metabolism of B[a]P. The tendency of fish to metabolize PAHs may explain why PAHs are frequently undetected or only detected in low concentrations in the livers of fish from environments heavily contaminated with PAHs.

A minimal amount of B[a]A is dissolved in the water column and degraded rapidly (half-life = several hours; EPA 1979b) by direct photolysis. Chemical oxidation may be a significant fate process for B[a]A in the water when chlorine or ozone (both oxidants) exist in sufficient concentrations (EPA 1979b).

The major fate of sediment-bound B[a]A, however, is most likely biodegradation. In general, the biodegradation processes are quite slow; a half-life of 7,000 h has been reported for B[a]A (EPA 1979b). Hinga and Pilson (1987) reported that after 2 months of biodegradation of sediment-bound B[a]A in an experimental marine ecosystem, neither B[a]A nor its degradation products appear to further degrade. Biodegradation in contaminated streams may be longer. These slow biodegradation rates indicate that B[a]A, and PAHs in general, are relatively persistent in the sediments of aquatic systems.

Within terrestrial systems also, biodegradation is the probable fate process. However, because this process is very slow, B[a]A is very persistent in soils. Bossert and Bartha (1986) reported that 90% of the original amount of B[a]A applied to soils existed after 11 months of incubation with bacteria. Coover and Sims (1987) estimated a half-life of 430 days for B[a]A in soil.

At hazardous waste sites, half-lives may be longer, as other contaminants present at the site may be toxic to the degrading microorganism. Bossert and Bartha (1986) reported reduced biodegradation of PAHs in soil containing a chemical toxic to microorganisms.

7. POTENTIAL FOR HUMAN EXPOSURE

7.1 OVERVIEW

As the previous discussions indicate, the greatest portion of environmental B[a]A releases are directly into the atmosphere. Consequently, inhalation is the primary route of background human exposure to B[a]A in the environment. Part of the B[a]A in the atmosphere returns to the surface via dry or wet deposition. This input, in addition to small direct releases by industry and publicly owned treatment works, leads to B[a]A in soil and water to which humans may be exposed. Humans also may be exposed to B[a]A in food, tobacco smoke, and some occupational environments, and through the use of PAH-containing products such as creosote, asphalt, and tar. At hazardous waste sites, humans most likely will be exposed to B[a]A in the soil and on particulate matter in air. At this time, B[a]A has been found at 62 of the 1,177 hazardous waste sites on the National Priorities List (NPL) in the United States (View 1989).

7.2 LEVELS MONITORED IN THE ENVIRONMENT

7.2.1 Air

Few data are available to characterize B[a]A levels in air, and estimates of ambient concentrations are limited to a small number of relatively outdated monitoring studies in Los Angeles, Baltimore, and Pittsburgh. Consequently, definitive statements about average background exposure levels cannot be made. In the most recent monitoring study, Gordon (1976) reported ambient B[a]A concentrations in Los Angeles County to range between 0.11 and 0.44 ng/m^3. This is somewhat lower than the values reported by Gordon and Bryan (1973), also in Los Angeles County. Based on monitoring data from 1971-1972, they reported B[a]A levels in the range of 0.04 to 3.1 ng/m^3. During this same time period, Fox and Staley (1976) reported average B[a]A concentrations of 4.6 ng/m^3 in College Park, Maryland. A much higher average concentration of 102 ng/m^3 was reported in the Baltimore Harbor Tunnel in Baltimore, Maryland. DeMaio and Corn (1966) reported B[a]A concentrations in Pittsburgh of approximately 63 ng/m^3.

7.2.2 Water

B[a]A has been detected in raw and finished drinking waters in the United States, but minimal data limit the degree to which background levels can be adequately characterized. Sorrell et al. (1981) reported B[a]A concentrations between 4 and 9 ng/L in raw water, and from <1 to 2 ng/L in finished drinking water. These data were based on a very small sample size (10 cities) and, therefore, are unlikely to be representative of drinking water concentrations in the United States.

7.2.3 Soil

No data are available on B[a]A levels in U.S. soils. However, Blumer et al. (1977) summarized data on the concentrations of total PAHs in soils and reported values between 4 and 13 mg/kg in the soil from relatively rural areas of the eastern United States. Soil levels in more populated and industrialized areas may be higher. Butler et al. (1984) examined soil PAH levels in Switzerland and demonstrated much higher soil B[a]A concentrations near complex road interchanges than at areas more distant. Also, the soils at waste sites, such as former manufactured-gas sites and creosote wood treatment plants may contain high levels of PAHs, including B[a]A.

7.2.4 Food

B[a]A has been detected in unprocessed cereal, vegetables, fruits, and in a variety of processed foods and beverages (IARC 1983). Based on limited data, EPA (1985) estimated a daily B[a]A intake from food of 30 ng. The method of preparation of certain foods can increase intake beyond this amount. For example, charcoal broiling increases the amount of B[a]A in meat. Lijinsky and Shubik (1965) measured an average of 230 ng B[a]A for approximately 6 ounces of charcoal-broiled steak (1,400 ng/kg of steak).

B[a]A also has been detected in vegetables and fruits grown in PAH-contaminated soil near high traffic areas (Wang and Meresz 1982) and in PAH-contaminated air (Grimmer 1979). Thus, consumption of food grown near contaminated areas, such as roadways, industrial areas, or hazardous waste sites, may contribute to human exposure.

Humans also may be exposed to B[a]A and other PAHs found in aquatic organisms that are typical components of the diet. Specifically, PAHs have been detected in bivalve mollusks (i.e., clams, oysters, mussels), crabs, and lobsters (Eisler 1987). PAHs also have been detected in fish; but fish levels are usually low, because this group rapidly metabolizes PAHs.

7.2.5 Cigarette Smoke

B[a]A has been reported to occur in cigarette mainstream smoke at between 20 and 70 ng/cigarette (DHHS 1986). Concentrations in sidestream smoke have been reported to be 2 to 4 times higher (DHHS 1986). Thus involuntary smokers, in addition to smokers, may receive elevated exposures to B[a]A from cigarettes.

7.3 OCCUPATIONAL EXPOSURES

PAHs, including B[a]A, have been isolated in numerous occupational situations, including coal-tar production and coking plants, coal gasification sites, smokehouses, aluminum production plants, asphalt and bitumen production plants, road and roof tarring activities, and around municipal incinerators. Historically, the highest level of human exposure to PAHs occurred in industrial situations. Concentrations of benzo[a]pyrene, often used as an indicator of total PAH concentration, have been reported to range from 800 to 23,100 ng/m^3 in the workroom air of coke oven operations in the United Kingdom (Davies et al. 1986).

Similarly high values have been reported by Lindstedt and Sollenberg (1982) in Swedish industries.

7.4 POPULATIONS AT HIGH RISK

At highest risk for cancer by PAHs are those people who are exposed to high levels of PAHs. Examples of high-risk populations include: workers in certain occupations that have elevated PAH concentrations in the ambient work environment; smokers and involuntary (passive) smokers who receive elevated PAH intake through tobacco smoke; and populations living near industries, such as creosote and coal tar manufacturers, that generate PAHs as a by-product of production.

Individuals in these high-exposure groups may have varying susceptibilities to PAH toxicity. Some of the available data on PAH carcinogenicity suggest a relationship between aryl hydrocarbon hydroxylase (AHH) activity and cancer risk. Genetic variation in AHH inducibility has been implicated as a determining factor for susceptibility to lung and laryngeal cancer (EPA 1980). Attempts have been made to demonstrate that persons with lung cancer have higher inducibility of AHH in cultured lymphocytes. A review by Calabrese (1984) indicates that several studies support this hypothesis, and some genetic data indicate that the human population can be segregated based upon this trait (EPA 1980). Thus, individuals that are AHH-inducible may constitute a special-risk population. However, the data regarding genetic susceptibility are not conclusive.

8. ANALYTICAL METHODS

8.1 ENVIRONMENTAL SAMPLES

The procedures used to sample and extract B[a]A in different media are very similar. In air and tobacco smoke, PAHs, including B[a]A, are adsorbed predominantly on particulate matter and the particulate matter is collected on a filter. In water and soil, PAHs are extracted without filtration.

The extraction of PAHs from the filter can be accomplished by a variety of techniques, with or without solvents. The following extraction techniques are the most commonly used: soxhlet, sublimation at elevated temperatures, ultrasonic, and polytron extraction (Sawicki 1976).

A cleanup step is necessary to separate B[a]A and PAHs from other pollutants. Typically, this step involves liquid-liquid extraction of the dry organic particulate extract, followed by adsorption chromatography using silica gel or alumina columns (Sawicki 1976, Riggin and Strup 1984). These adsorbents selectively remove interfering compounds. In addition, thin-layer chromatography can be used as a cleanup method (Sawicki 1976).

The most commonly used analytical methods for determining B[a]A in environmental samples are column gas chromatography (GC) and high-performance liquid chromatography (HPLC). Table 8.1 summarizes common analytical methods, detection limits, and accuracy (percent recovery) for the determination of B[a]A in air, water, soil, and food.

Column gas chromatography (GC) is an analytical technique in which components of a sample are separated by differential distribution between a gaseous mobile phase and a solid or liquid stationary phase (EPA 1983). Following separation in the GC column, sample components are identified and quantified by a detection system such as flame ionization detection (FID), ultraviolet absorption spectroscopy (UV), or mass-spectrometry (MS). These techniques are detailed in NIOSH (1984) and EPA (1983, 1984a).

HPLC is an analytical method in which components are separated based on their polarity (EPA 1983). Reverse-phase HPLC, which is used more widely for the analysis of PAHs, uses a nonpolar stationary phase and a polar mobile phase; hydrophilic components are eluted earlier than hydrophobic components. The detection systems most appropriate for HPLC analysis of PAHs are UV absorption spectroscopy and fluorescence spectroscopy (FS). Das and Thomas (1978) examined the use of both a UV and a fluorescence detector for determination of PAHs following HPLC. The UV detection system failed to resolve B[a]A from chrysene in a multicomponent mixture. However, by selection of excitation and emission

Table 8.1. Methods for analysis of benz(a)anthracene in environmental media

Medium	Sample preparation	Analytical method[a]	Detection limit	Accuracy[b]	References
Air	Ultrasonic extraction with cyclohexane	HPLC	3 ng/m³ (1500-m³ sample)	95%	NIOSH 1984 (Method 5506)
	Ultrasonic extraction with benzene, pentane, or dichloromethane	HPLC/FS	10 pg	NA	Andersson et al. 1983
	Soxhlet extraction with benzene/methanol	GC/MS	0.05 ng/m³	NA	Matsumoto and Kashimoto 1985
	Extraction with solvent	GC/MS	NA	NA	NIOSH 1984 (Method 5515)
Water	Extraction with methylene chloride	HPLC/FS	0.013 µg/L	~73%[c]	EPA 1984a (Method 610)
		UV	4 µg/L	76 to 135%	Riggin and Strup 1984
	Extraction with methylene chloride at pH ≤2 and pH ≥11	GC/MS	7.8 µg/L	~90%[c]	EPA 1984a (Method 625)
	Extraction with methylene chloride at pH 12 to 13 and pH <2	GC/MS	10 µg/L	NA	EPA 1984a (Method 1625)
		GC/MS	NA	NA	EPA 1986a
	Extraction with dichloromethane	HPLC/UV	35 pg	NA	Ogan et al. 1979
	Extraction with cyclohexane	TLC/FS	0.5 to 1 ng/L	NA	Borneff and Kunte 1979
Soil	Extraction with *n*-pentane	TLC/UV	NA	NA	Butler et al. 1984
	Extraction with methylene chloride	GC/MS	NA	NA	EPA 1986a
Food	Extraction with isooctane	TLC/UV	0.2 µg/kg	NA	Howard 1979

[a]Abbreviations: HPLC, high-performance liquid chromatography; TLC, thin-layer chromatography; FS, fluorescence spectroscopy; GC, column gas chromatography; MS, mass spectrometry; UV, ultraviolet absorption spectroscopy.

[b]NA = Not available.

[c]In large samples.

wavelengths, fluorescence spectroscopy can obtain resolution of both B[a]A and chrysene.

Thin-layer chromatography (TLC) has also been used to analyze for PAHs. With quasi-linear luminescence methods (QLL), quasi-linear spectra can be obtained for PAHs at liquid nitrogen temperatures (Sawicki 1976).

GC and HPLC are the chromatographic methods routinely used for the determination of 10 to 20 of the major PAHs in air and water samples. Detailed analysis of major and minor PAHs in a complex PAH mixture requires a combination of chromatographic techniques (Wise et al. 1986). GC/MS has a detection limit of greater than 10 pg; HPLC/FS has an approximate detection limit for PAHs of 25 to 50 pg (Santodonato et al. 1981). Das and Thomas (1978) reported that fluorescence spectroscopy used with HPLC results in separation of B[a]A from chrysene. Das and Thomas (1978) reported a detection limit (twice the signal-to-noise ratio) of 0.6 pg for B[a]A from a synthetic PAH mixture.

HPLC (5506) or GC/MS (5515) are the methods recommended by NIOSH for analyzing PAHs in workplace air (NIOSH 1984). These methods incorporate a sampling train consisting of a filter and a solid sorbent (NIOSH 1984). The use of a high-volume sampler to sample a large quantity of air allows for detection of small amounts of PAH. The analytical methods required by EPA (1984a) for the analysis of B[a]A in water are procedures 610 (HPLC/FS), 625 (GC/MS), and 1625 (GC/MS). These are required test procedures for municipal and industrial wastewater-discharging sites under the Clean Water Act. GC/MS is the method required by the EPA Contract Laboratory Program for analysis of B[a]A and other PAHs in water and soil. The contract required quantitation limit (CRQL) for B[a]A in water is 10 µg/L, and that in soil/sediment is 330 µg/kg (EPA 1986a).

8.2 BIOLOGICAL SAMPLES

The available biological monitoring techniques are useful for detecting whether occupational or environmental exposure to PAHs has occurred; however, because there have been no population-based studies to determine normal body levels of PAHs, it is not yet possible to predict environmental exposure from body PAH levels or to predict what health effects are likely to be associated with these levels. In general, techniques that measure PAH or PAH metabolite concentration in the urine are most appropriate for use in determining occupational exposure, since a high level of PAH exposure is necessary to result in the presence of these compounds in the urine. Methods that detect diol expoxide-DNA adducts are more sensitive to low exposure levels and are most appropriate for use in determining environmental exposure. The techniques presently available for determining exposure to PAHs are summarized in Table 8.2 and discussed in detail below.

Modica et al. (1982) and Bartosek et al. (1984) examined PAHs present in blood, mammary, adipose, liver, and brain tissue from orally exposed rats using gas-liquid chromatography with a flame-ionization detector. B[a]A was determined in all tissues examined. Examples of determination of B[a]A concentrations in human tissue samples using this technique were not located in the available literature. The detection limit for this method was not reported.

Table 8.2. Methods for analysis of PAHs in biological samples

Medium	Technique	Measured parameter	References
Tissue	Gas chromatography	PAH concentration	Modica et al. 1982, Bartosek et al. 1984
	Postlabeling of DNA	PAH diol epoxide DNA adducts	Randerath et al. 1985, Randerath et al. 1986
Blood	Immunoassay	Antibodies to diol epoxide-DNA adducts	Harris 1985, Harris et al. 1986
Urine	Gas chromatography	PAH concentration	Clonfero et al. 1986
	High-performance liquid chromatography	PAH concentration	Becher and Bjorseth 1983, Becher et al. 1984

In mammalian systems, B[a]A is converted by specific cellular enzymes to *trans*-dihydrodiols. These dihydrodiols are further converted to diol epoxides that are capable of binding to DNA. Phenolic derivatives formed from rearrangement of the epoxides or from acid-catalyzed dehydration of the *trans*-dihydrodiols can be separated and quantified using HPLC/UV in vitro (Mushtaq et al. 1987). Separation of the enantiomeric *trans*-dihydrodiols of B[a]A is also a potential method of determining biological exposure to B[a]A (Yang et al. 1984, Chiu and Yang 1986). The degree of DNA adduct formation can be used as a measure of dose in target tissues or organs. Randerath et al. (1985, 1986) examined PAH-DNA adducts in skin tissue from mice dermally treated with cigarette smoke condensate and in placenta, bronchus, and larynx tissue from smokers. In this technique, radioactivity (^{32}P) is incorporated into the DNA removed from the exposed cells and the digested DNA is separated using thin-layer chromatography. Quantitation of the adducts is achieved by scintillition counting. Small amounts of DNA are needed for analysis. These techniques have not been examined in humans or in actual biological samples to determine whether abnormal levels can be detected.

Procedures are currently available that examine the presence of antibodies to PAH-DNA adducts in the blood using enzymatic immunoassays (Harris 1985, Harris et al. 1986). Harris et al. (1986) examined human sera from coke oven workers, individuals exposed to ambient levels of PAHs, and individuals with carcinoma of the lung for the presence of antibodies to PAH-DNA adducts, including B[a]A-DNA adducts. Positive sera contained antibodies to each PAH individually or antibodies to epitopes common to the PAHs. Positive sera were found in 25% of the coke oven workers, 33% of the control individuals, and 57% of the cancer patients. However, because of the high percentage of control individuals with positive sera, the sensitivity of the technique may be limited. Harris (1985) developed a technique for determining human exposure to PAHs by detecting antibodies in sera to diol epoxide-DNA adducts using immunoassay. The technique was tested on coke oven workers exposed to substantial amounts of benzo[a]pyrene and other PAHs in the work atmosphere, smokers, and nonsmokers. Antibodies to benzo[a]pyrene diol epoxide-DNA adducts were quantified by enzyme-linked immunosorbent assay (ELISA). Higher proportions of sera positive for antibodies were found in a group of smokers and in the occupationally exposed group.

The urine of exposed humans was examined for the presence of B[a]A. PAHs and their metabolites can be extracted from urine and analyzed using HPLC/FS or GC/MS. B[a]A was found in the urine of workers exposed to PAHs in an aluminum plant. However, environmental exposure could not be determined from urine chrysene content, because high environmental concentrations of PAHs in the workplace were not found to be reflected to the same extent in excretion of PAHs in the urine (Becher and Bjorseth 1983, Becher et al. 1984). This problem was suggested to result from the nonbioavailability of particle-bound B[a]A, and this method may still be applicable in other exposure situations. Clonfero et al. (1986) detected B[a]A using GC/MS in the urine of individuals treated therapeutically with crude coal tar. However, this is not necessarily a useful test for occupational exposure, because high levels of PAHs in the coal tar were necessary to concentrate PAHs in the urine.

Vo-Dinh et al. (1987) developed an antibody-based fiber-optic biosensor that can be used to detect benzo[a]pyrene or other PAHs in sample solutions. In this technique, antibodies to benzo[a]pyrene are covalently bound to the tip of the sensing probe. A helium-cadmium laser excites the molecules of benzo[a]pyrene bound to the antibodies, and the resulting fluorescence of these molecules is recorded by a photomultiplier; the intensity of the fluorescence signal is proportional to the amount of antigen bound to the sensor tip. The fiber-optic device can detect 1 femtomole (fmol; one-quadrillionth of a mole) of benzo[a]pyrene in a 5-μL sample drop. This technique can be useful in the assessment of exposure of an individual to benzo[a]pyrene and other PAHs, provided appropriate antibodies are used.

9. REGULATORY AND ADVISORY STATUS

Regulatory standards have been developed for the carcinogenic PAHs based on the benzene or cyclohexane soluble fraction of coal tar pitch volatiles containing anthracene, benzo[a]pyrene, phenanthrene, acridine, chrysene, and pyrene. Therefore, these standards are not specific for B[a]A. However, the regulatory standards were developed to regulate exposures to PAHs in coal tar pitch volatiles and are presented in Table 9.1.

B[a]A has been shown to be carcinogenic in experimental animals and undergoes metabolism to reactive electrophiles capable of binding covalently to DNA and inducing bacterial mutation and DNA damage. IARC (1973) has classified B[a]A in Group 2B, because of sufficient evidence of carcinogenicity in experimental animals. IARC (1985) has also concluded that there is sufficient evidence of carcinogenicity of coal tars, creosote, and coal tar pitches in experimental animals. In addition, IARC concluded that there is sufficient evidence that occupational exposure to coal tar and coal tar pitch is associated with skin cancer and limited evidence of the carcinogenicity of creosote in occupationally exposed individuals.

9.1 INTERNATIONAL

The World Health Organization European standards for drinking water recommend a concentration of PAHs not to exceed 0.2 μg/L. This is based on the composite of six PAHs in drinking water: fluoranthene, benzo[a]pyrene, benzo[g,h,i]perylene, benzo[b]fluoranthene, benzo[k]fluoranthene, and indeno[1,2,3-cd]pyrene (WHO 1971). This limit was not chosen on the basis of potential health effects.

9.2 NATIONAL

9.2.1 Regulatory Standards

Coal tar, coal tar pitch, and creosote are considered by NIOSH and EPA to be human carcinogens (NIOSH 1977; EPA 1978, 1981, 1984c, 1986b). NIOSH reviewed epidemiologic and experimental toxicological evidence and concluded that inhalation exposure to these coal products, which contain a number of PAHs, increases the risk of lung and skin cancer in workers (NIOSH 1977). The Secretary of Labor has taken the position that no safe occupational exposure can be established for a carcinogen.

The current workroom air standard determined by OSHA is an 8-h time-weighted average permissible exposure limit (PEL) of 0.2 mg/m^3 for the benzene-soluble fraction of coal tar pitch volatiles (OSHA 1985). The PEL was established to minimize exposure to those PAHs believed to be carcinogens.

Table 9.1. Regulatory standards and advisory levels

Regulatory standard or advisory level	Basis	Concentration or risk coefficient	References
	Air		
Regulatory standard:			
8-h Time-weighted average permissible exposure limit (PEL)	Benzene-soluble fraction of coal tar pitch volatiles	0.2 mg/m^3	OSHA 1985
Advisory levels:			
8-h Time-weighted average threshold limit value	Benzene-soluble fraction of coal tar pitch volatiles	0.2 mg/m^3	ACGIH 1986
10-h Time-weighted average threshold limit value	Cyclohexane-soluble fraction of coal tar pitch volatiles	0.1 mg/m^3	NIOSH 1977
	Water		
Advisory levels:			
Ambient water quality criterion	Total carcinogenic PAHs	0 (28, 2.8, and 0.28 ng/L)[a]	EPA 1980

[a]The EPA recommended concentration for ambient water is zero. However, because attainment of this level may not be possible to achieve, the EPA estimated concentrations of total carcinogenic PAHs for ambient water corresponding to a 10^{-5}, 10^{-6}, and 10^{-7} upper-bound lifetime excess risk estimate, respectively, are presented.

9.2.2 Advisory Levels

9.2.2.1 Air advisory levels

ACGIH Time-Weighted Average Threshold Limit Value. The American Conference of Governmental Industrial Hygienists (ACGIH 1986) recommended a time-weighted average threshold limit value (TLV) for occupational exposure to coal tar pitch volatiles based on an 8-h workday and 40-h workweek. The ACGIH time-weighted average TLV of 0.2 mg/m^3 is based on the benzene-soluble fraction of coal tar pitch volatiles (including benzo[a]pyrene, anthracene, phenanthrene, acridine, chrysene, and pyrene). The TLV is based on the ACGIH conclusion that at concentrations below 0.2 mg/m^3, any increase in the incidence of lung and other tumors caused by occupational exposure to coal tar pitch volatiles should be minimal.

NIOSH Time-Weighted Average Threshold Limit Value. The National Institute for Occupational Safety and Health (NIOSH) examined the epidemiologic and experimental toxicological evidence on coal tar, coal tar pitch, and creosote, and concluded that they are carcinogenic to experimental animals and potentially to humans (NIOSH 1977). PAHs have been identified in coal tar products. Because of the carcinogenic potential of these compounds, NIOSH recommended that the PEL be set at the lowest concentration detected by the NIOSH-recommended method of environmental monitoring, 0.1 mg/m^3 (NIOSH 1977). NIOSH proposed this time-weighted average TLV to reduce the risk of cancer associated with exposure to coal tar products in the workplace.

9.2.2.2 Water advisory levels

Ambient Water Quality Criterion. EPA (1980) developed an ambient water quality criterion (AWQC) to protect human health from the potential carcinogenic effects caused by exposure to carcinogenic PAHs through ingestion of contaminated water and contaminated aquatic organisms.

B[a]A is a known animal carcinogen. Because there is no recognized safe concentration for a human carcinogen, EPA (1980) recommended that the sum of the concentrations of total carcinogenic PAHs in ambient water be zero. However, EPA (1980) recognized that a zero concentration level may not be possible to attain. The present criterion for total carcinogenic PAHs was developed using the carcinogenicity assay reported by Neal and Rigdon (1967) in which stomach tumors developed in CFW-Swiss mice exposed to doses of 1 to 250 ppm benzo[a]pyrene in the diet with a statistically higher incidence than controls. Assuming that an individual consumes 2 L of water and 6.5 g of fish and shellfish each day, the sum of the concentrations of total carcinogenic PAHs corresponding to upper-bound lifetime excess cancer risks of 10^{-5}, 10^{-6} and 10^{-7} are 28, 2.8, and 0.28 ng/L, respectively.

9.2.2.3 Food advisory levels

No food advisory levels for B[a]A were located in the available literature.

9.2.2.4 Other guidance

Sections 103(a) and 103(b) of the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA) require that persons in charge of vessels or facilities from which a hazardous substance has been released in quantities that are equal to or greater than its reportable quantity (RQ) immediately notify the National Response Center of the release. Potential carcinogens are grouped into high-, medium-, or low-hazard categories on the basis of biological information available. The RQ for B[a]A is 1 lb (EPA 1987).

9.2.3 Data Analysis

9.2.3.1 Carcinogenic potency

Although EPA previously published inhalation and oral cancer risk estimates for benzo[a]pyrene (EPA 1984b) based on the studies of Thyssen et al. (1981) and Neal and Rigdon (1967), these numbers are currently under review and have not been included here pending recalculation.

9.3 STATE

The state of New York has recommended a guidance level of 0.2 μg/L for the sum of benz[a]anthracene, benzofluoranthene, benzo[a]pyrene, chrysene, fluoranthene, indeno[1,2,3-cd]pyrene, methylbenz[a]anthracene, and pyrene in ambient water (NYSDEC 1984). (Regulations and advisory guidance from the states were still being compiled at the time of printing.)

10. REFERENCES

Aldrich Chemical Company. 1986. Catalog of Fine Chemicals. Aldrich Chemical Co., Milwaukee, Wis.

Allen-Hoffman BL, Rheinwald JG. 1984. Polycyclic aromatic hydrocarbon mutagenesis of human epidermal keratinocytes in culture. PNAS Biol 81:7802-7806.

Amacher DE, Turner GN. 1980. Promutagen activation by rodent-liver postmitochondrial fractions in the L5178Y/TK cell mutation assay. Mutat Res 74:485-501.

Amacher DE, Paillet SC. 1983. The activation of procarcinogens to mutagens by cultured rat hepatocytes in the L5178Y/TK mutation assay. Mutat Res 113:77-88.

Amacher DE, Paillet SC, Turner GN, Ray VA, Salsburg DS. 1980. Point mutations at the thymidine kinase locus in L5178Y mouse lymphoma cells. II. Test validation and interpretation. Mutat Res 72:447-474.

ACGIH (American Conference of Governmental Industrial Hygienists). 1986. Threshold Limit Values and Biological Exposure Indices. 5th ed. ACGIH, Cincinnati, Ohio.

Andersson K, Levin J-O, Nilsson C-A. 1983. Sampling and analysis of particulate and gaseous polycyclic aromatic hydrocarbons from coal tar sources in the working environment. Chemosphere 12:197-207.

Barnes D et al. 1987. Reference dose (RfD): Description and use in health risk assessments. Appendix A in the Integrated Risk Information System Supportive Documentation, Vol. 1. Office of Health and Environmental Assessment, Environmental Protection Agency, Washington, D.C., EPA/600/8-86/032a.

Barofsky DF, Baum EJ. 1976. Exploratory field desorption mass analysis of the photoconversion of adsorbed polycyclic aromatic hydrocarbons. J Am Chem Soc 98:25-26.

---

*Key studies.

Bartosek I, Guaitani A, Modica R, Fiume M, Urso R. 1984. Comparative kinetics of oral benz[a]anthracene, chrysene, and triphenylene in rats: Study with hydrocarbon mixtures. Toxicol Lett 23:333-339.

Bartsch H, Malaveille C, Camus A-M, et al. 1980. Validation and comparative studies on 180 chemicals with *S. typhimurium* strains and V79 Chinese hamster cells in the presence of various metabolizing systems. Mutat Res 76:1-50.

Basler A, Rohrborn G. 1978. Mutagenicity of polycyclic hydrocarbons. IV. Correlated studies with anthracene, benzo[a]anthracene, B[a]P, chrysene, and phenanthrene. Proc Perugia Qudrenn Int Conf Cancer 6:843-849.

* Becher G, Bjorseth A. 1983. Determination of exposure to polycyclic aromatic hydrocarbons by analysis of human urine. Cancer Lett. 17:301-311.

Becher G, Haugen A, Bjorseth A. 1984. Multimethod determination of occupational exposure to polycyclic aromatic hydrocarbons in an aluminum plant. Carcinogenesis 5:647-651.

Benedict WF, Gielen JE, Nebert DW. 1972. Polycyclic hydrocarbon-produced toxicity, transformation, and chromosomal aberrations as a function of aryl hydrocarbon hydroxylase activity in cell culture. Int J Cancer 9(2):435-451.

* Bingham E, Falk HL. 1969. The modifying effect of carcinogens on the threshold response. Arch Environ Health 19:779-783.

Blumer M, Blumer W, Reich T. 1977. Polycyclic aromatic hydrocarbons in soils of a mountain valley: Correlation with highway traffic and cancer incidence. Environ Sci Technol 11:1082-1084.

* Bock FG, Burnham M. 1960. The effect of experimental conditions upon the concentration of hydrocarbon in mouse skin after cutaneous application. Cancer Res 21:510-515.

Bock FG, King DW. 1959. A study of the sensitivity of the mouse forestomach toward certain polycyclic hydrocarbons. J Natl Cancer Inst 23:833.

Bock FG, Mund R. 1958. A survey of compounds for activity in the suppression of mouse sebaceous glands. Cancer Res 18:887-892.

Borneff J, Kunte H. 1979. Analysis of polycyclic aromatic hydrocarbons in water using thin layer chromatography and spectrofluorometry. In: Egan H, ed. Environmental Carcinogens: Selected Methods of Analysis. Vol. 3. Analysis of Polyaromatic Hydrocarbons in Environmental Samples. IARC, Lyon, France, pp. 129-139.

Bossert ID, Bartha R. 1986. Structure-biodegradability relationship of polycyclic aromatic hydrocarbons in soil. Bull Environ Contam Toxicol 37:490-495.

Boyland E, Sims P. 1964. Metabolism of polycyclic compounds. 24. The metabolism of benz[a]pyrene. Biochem J 91:493-506.

Boyland E, Sims P. 1965. The metabolism of benz[a]anthracene and dibenz[a,h]anthracene and their 5,6-epoxy-5,6-dihydro derivatives by rat-liver homogenates. Biochem J 97:7-16.

Brendel M, Ruhland A. 1984. Relationships between functionality and genetic toxicology of selected DNA-damaging agents. Mutat Res 133:51-85.

Butler JD, Butterworth V, Kellow C, Robinson HG. 1984. Some observations on the polycyclic aromatic hydrocarbon (PAH) content of surface soils in urban areas. Sci Total Environ 38:75-85.

Calabrese EJ. 1984. Ecogenetics: Genetic Variation in Susceptibility to Environmental Agents. John Wiley and Sons, New York.

Chiu P-L, Yang SK. 1986. Liquid chromatographic separation of five *trans*-dihydrodiols of benz[a]anthracene. J Liq Chromatogr 9:701-709.

Clive D, Johnson KO, Spector JFS, Baston AG, Brown MMM. 1979. Validation and characterization of the L5178y/TK+/1- mouse lymphoma mutagen assay system. Mutat Res 59:61.

* Clonfero E, Zordan M, Cottica D, et al. 1986. Mutagenic activity and polycyclic aromatic hydrocarbon levels in urine of humans exposed to therapeutical coal tar. Carcinogenesis 7:819-823.

Conney AH. 1982. Induction of microsomal enzymes by foreign chemicals and carcinogenesis by polycyclic aromatic hydrocarbons: G.H.A. Clowes Memorial Lecture. Cancer Res 42:4875-4917.

Cookson HA. 1924. Epithelioma of the skin after prolonged exposure to creosote. Br Med J 68(1):368.

Coombs MM, Dixon C, Kissonerghis A-M. 1976. Evaluation of the mutagenicity of compounds of known carcinogenicity, belonging to the benz[a]anthracene, chrysene, and cyclopenta[a]phenanthrene series, using Ames test. Cancer Res 36:4525-4529.

Cooper CS, Grover PL, Sims P. 1983. The metabolism and activation of benzo[a]pyrene. In: Bridges JW, Chase LF, eds. Progress in Drug Metabolism. Vol. 7. John Wiley and Sons, New York, pp. 295-395.

* Coover MP, Sims RC. 1987. The effects of temperature on polycyclic aromatic hydrocarbon persistence in an unacclimated agriculture soil. Haz Waste Haz Mat 4:69-82.

CRC Handbook of Chemistry and Physics. 1987. 6th ed. CRC Press, Boca Raton, Fla.

Creasia DA, Poggenburg JK, Jr, Nettesheim P. 1976. Elution of benzo[a]pyrene from carbon particles in the respiratory tract of mice. J Toxicol Environ Health 1:967-975.

Das BS, Thomas GH. 1978. Fluorescence detection in high performance liquid chromatographic determination of polycyclic aromatic hydrocarbons. Anal Chem 967-973.

* Davies GM, Hodkinson A, DiVetta P. 1986. Measurement and analysis of occupational exposure to coke oven emissions. Ann Occup Hyg 30:51-62.

DeMaio L, Corn M. 1966. Polynuclear aromatic hydrocarbons associated with particulates in Pittsburgh air. JAPCA 16:67-71.

DenHollander H, VanDeMeet D, VanNoort P, Wondergem E. 1986. Wet deposition of polycyclic aromatic hydrocarbons in the Netherlands. Sci Total Environ 52:211-219.

DHHS (Department of Health and Human Services). 1986. The Health Consequences of Involuntary Smoking, a Report of the Surgeon General. Office on Smoking and Health, Rockville, Md.

DiPaolo JA, Donovan JP, Nelson RL. 1969. Quantitative studies of in vitro transformation by chemical carcinogens. J Natl Cancer Inst 42:867-874.

DiPaolo JA, Donovan JP, Nelson RL. 1971. Transformation of hamster cells in vitro by polycyclic hydrocarbons without cytotoxicity. Proc Natl Acad Sci USA 68:2958-2961.

Dunkel VC, Pienta RJ, Sivak A, Traul KA. 1981. Comparative neoplastic transformation responses of BALb 3T3 cells, Syrian hamster embryo cells, and Rauscher murine leukemia virus-infected Fisher 344 rat embryo cells to chemical carcinogens. J Natl Cancer Inst 67:1303-1315.

Dunkel VC, Zeiger E, Brusick D, et al. 1984. Reproducibilty of microbial mutagenicity assays: Tests with *Salmonella typhimurium* and *Escherichia coli* using a standardized protocol. Environ Mutagenesis 6:1-251.

Eisler R. 1987. Polycyclic Aromatic Hydrocarbon Hazards to Fish, Wildlife, and Invertebrates. A Synoptic Review. Biological Rep 85. Contam Haz Rev Rep 11. U.S. Fish and Wildlife Service, U.S. Department of the Interior.

EPA (Environmental Protection Agency). 1978. Notices of Rebuttable Presumption Against Registration and Continued Registration (RPAR) of Pesticide Products Containing Coal Tar, Creosote, and Coal Tar Neutral Oils. Position Document (PD) 1. Office of Pesticide Programs, Washington, DC.

EPA (Environmental Protection Agency). 1979a. Toxic Substances Control Act Chemical Substances Inventory. Volume E. Office of Toxic Substances, Washington, D.C., EPA-TSCA-/CSI-VI.

* EPA (Environmental Protection Agency). 1979b. Water-Related Environmental Fate of 129 Priority Pollutants. Washington, D.C., December 1979, EPA 440/4-79-029.

EPA (Environmental Protection Agency). 1980. Ambient Water Quality Criteria for Polynuclear Aromatic Hydrocarbons. Office of Water Regulations and Standards, Washington, D.C., EPA 440/5-80-069, NTIS PB81-117806.

EPA (Environmental Protection Agency). 1981. Wood Preservative Pesticides. Creosote, Pentachlorophenol, and the Inorganic Arsenicals (Wood Uses). Position Document (PD) 2/3. Office of Pesticide Programs, Washington, D.C.

EPA (Environmental Protection Agency). 1982. Aquatic Fate Process Data for Organic Priority Pollutants. Office of Water Regulations and Standards, Washington, D.C., EPA 440/4-81-014.

EPA (Environmental Protection Agency). 1983. Technical Assistance Document for Sampling and Analysis of Toxic Organic Compounds in Ambient Air. Environmental Monitoring Systems Laboratory, Research Triangle Park, N.C., June 1983, EPA 600/4-83-027.

EPA (Environmental Protection Agency). 1984a. Guidelines establishing test procedures for the analysis of pollutants under the Clean Water Act; final rule and interim final rule and proposed rule. Fed Regist 49:1-210 (Oct. 26, 1984).

EPA (Environmental Protection Agency). 1984b. Health Effects Assessment for Polycyclic Aromatic Hydrocarbons (PAH). Environmental Criteria and Assessment Office, Cincinnati, Ohio, EPA 540/1-86-013.

EPA (Environmental Protection Agency). 1984c. Wood Preservative Pesticides: Creosote, Pentachlorophenol, and Inorganic Arsenicals. Position Document (PD4). Office of Pesticide Programs, Washington, D.C., July 1984, NTIS TB-84-241538.

* EPA (Environmental Protection Agency). 1985. An Exposure and Risk Assessment for Benzo[a]pyrene and Other Polycyclic Aromatic Hydrocarbons. Vol. IV. Office of Water, Washington, D.C., EPA 440/4-85-020-V4.

EPA (Environmental Protection Agency). 1986a. Statement of Work for Organics Analysis. EPA Contract Laboratory Program, October 1986.

EPA (Environmental Protection Agency). 1986b. Creosote, pentachlorophenol, and inorganic arsenicals: Amendment of notice of intent to cancel registrations. Fed Regist 51:1334 (Jan. 10, 1986).

EPA (Environmental Protection Agency). 1987. 40 CFR Parts 117 and 302. Reportable quantity adjustments. Fed Regist 52:8140-8153 (Mar. 16, 1987).

Fahl WE, Scarpelli DS, Gill K. 1981. Relationship between B[a]P-induced DNA base modification and frequency of reverse mutations in mutant strains of *Salmonella typhimurium*. Cancer Res 41:3400-3406.

Fahmy OG, Fahmy MJ. 1973. Oxidative activation of benz[a]anthracene and methylated derivatives in mutagenesis and carcinogenesis. Cancer Res 33:2354-2361.

Fahmy MJ, Fahmy OG. 1980. Altered control of gene activity in the soma by carcinogens. Mutat Res 72:165-172.

Fox MA, Staley SW. 1976. Determination of polycyclic aromatic hydrocarbons in atmospheric particulate matter by high pressure liquid chromatography coupled with fluorescence techniques. Anal Chem 48:992-998.

Freeman AE, Weisburger EK, Weisburger JH, Wolford RG, Maryak JM, Huebner RJ. 1973. Transformation of cell cultures as an indication of the carcinogenic potential of chemicals. J Natl Cancer Inst 51:799-808.

* Gordon RJ. 1976. Distribution of airborne polycyclic aromatic hydrocarbons throughout Los Angeles. Environ Sci Technol 10:370-373.

* Gordon RJ, Bryan RJ. 1973. Patterns in airborne polynuclear hydrocarbon concentrations at four Los Angeles sites. Environ Sci Technol 7:1050-1053.

Grimmer G. 1979. Sources and occurrence of polycyclic aromatic hydrocarbons. In: Egan H, ed. Environmental Carcinogens Selected Methods of Analysis. Vol. 3. IARC Publ 29. International Agency for Research on Cancer, Lyon, France.

* Habs M, Schmahl D, Misfeld J. 1980. Local carcinogenicity of some environmentally relevant polycyclic aromatic hydrocarbons after lifelong topical application to mouse skin. Arch Geschwulstforsch 50:266-274.

Hammond ED, Selikoff IJ, Lawther PO, Seidman H. 1976. Inhalation of B[a]P and cancer in man. Ann NY Acad Sci 271:116-124.

Harris CC, Sporn MB, Kaufman DG, Smith JM, Baker MS, Saffiotti V. 1971. Acute ultrastructural effects of benzo[a]pyrene and ferric oxide on the hamster tracheobronchial epithelium. Cancer Res 31:1977.

* Harris C. 1985. Method and Kit for Detecting Human Exposure to Genotoxic Agents. U.S. Department of Health and Human Services, Washington, D.C., PAT-APPL-6-778-669, PB86-131620.

* Harris CC, Newman MJ, Weston A, Mann DL. 1986. Identification of human antibodies to polycyclic aromatic hydrocarbon-DNA adducts. Clin Res 34:690A.

HSDB (Hazardous Substances Databank). 1987. Benz[a]anthracene. National Library of Medicine, Toxicology Information Program.

Henry SA. 1947. Occupational cutaneous cancer attributable to certain chemicals in industry. Br Med Bull 4:398-401.

Hinga KR, Pilson ME. 1987. Persistence of benz[a]anthracene degradation products in an enclosed marine ecosystem. Environ Sci Technol 21:648-653.

Howard J. 1979. Analysis of B[a]P and other polycyclic aromatic hydrocarbons in food. In: Egan H, ed. Environmental Carcinogens: Selected Methods of Analysis. Vol. 3. Analysis of Polyaromatic Hydrocarbons in Environmental Samples. IARC, Lyon, France, pp. 175-191.

Huberman E. 1975. Mammalian cell transformation and cell-mediated mutagenesis by carcinogenic polycyclic hydrocarbons. Mutat Res 29:285-291.

Huberman E, Sachs L. 1974. Cell-mediated mutagenesis of mammalian cells with chemical carcinogens. Int J Cancer 13:326:333.

Huberman E, Sachs L. 1976. Mutability of different genetic loci in mammalian cells by metabolically activated carcinogenic polycyclic hydrocarbons. Proc Natl Acad Sci USA 73:188-192.

Huberman E, Kuroki T, Marquardt H, et al. 1972. Transformation of hamster embryo cells by epoxides and other derivatives of polycyclic hydrocarbons. Cancer Res 32:1391-1396.

IARC (International Agency for Research on Cancer). 1973. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man. Vol. 3. Certain Polycyclic Aromatic Hydrocarbons and Heterocyclic Compounds. IARC, Lyon, France, pp. 46-68.

IARC (International Agency for Research on Cancer). 1983. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Vol. 32. Polynuclear Aromatic Compounds, Part 1. Chemical, Environmental, and Experimental Data. IARC, Lyon, France.

IARC (International Agency for Research on Cancer). 1984. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. Vol. 34. Polynuclear Aromatic Compounds, Part 3, Industrial Exposures in Aluminum Production, Coal Gasification, Coke Production, and Iron and Steel Founding. IARC, Lyon, France.

IARC (International Agency for Research on Cancer). 1985. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. Vol. 35. Polynuclear Aromatic Compounds, Part 4, Bitumens, Coal Tars and Derived Products, Shale Oils, and Soots. IARC, Lyon, France.

Ide F, Ishikawa T, Takayama S. 1981. Detection of chemical carcinogens by assay of unscheduled DNA synthesis in rat tracheal epithelium in short-term organ culture. J Cancer Res Clin Oncol 102:115-126.

Kaden DA, Hites RA, Thilly WG. 1979. Mutagenicity of soot and associated polycyclic aromatic hydrocarbons to *Salmonella typhimurium*. Cancer Res 39:4152-4159.

* Kamens RM, Fulcher JN, Zhishi G. 1986. Effects of temperature on wood soot PAH decay in atmospheres with sunlight and low NO_x. Atmos Environ 20:1579-1587.

* Kao JK, Patterson FK, Hall LJ. 1985. Skin penetration and metabolism of topically applied chemicals in six mammalian species, including man: An in vitro study with benzo[a]pyrene and testosterone. Toxicol Appl Pharmacol 81:502-516.

Kennaway NM, Kennaway EL. 1936. Study of the incidence of cancer of the lung and larynx. J Hyg 36:236-267.

Keysell GR, Booth J, Sims P. 1975. Glutathione conjugates as metabolites of benz[a]anthracene. Xenobiotica 5:439-447.

* Klein M. 1963. Susceptibility of strain B6AF/J hybrid infant mice to tumorigenesis with 1,2-benzanthracene, deoxycholic acid, and 3-methylcholanthrene. Cancer Res 23:1701-1707.

Kochlar TS. 1982. Effects of polycyclic hydrocarbons on the induction of chromosomal aberrations in the absence of an exogenous metabolic activation system in cultured hamster cells. Experentia 38:845-846.

Korfmacher WA, Natusch DFS, Taylor DR, Mamantov G, Wehry EL. 1980a. Oxidative transformation of polycyclic aromatic hydrocarbons adsorbed on coal fly ash. Science 207:763-765.

Korfmacher WA, Wehry EL, Mamantov G, Natusch DFS. 1980b. Resistance to photochemical decomposition of polycyclic aromatic hydrocarbons vapor-adsorbed on coal fly ash. Environ Sci Technol 14:1094-1099.

Kouri RE, Rude TH, Joglekar R, et al. 1978. 2, 3, 7, 8-Tetrachlorodibenzo-p- dioxin as cocarcinogen causing 3-methylcholanthrene initiated subcutaneous tumors in mice genetically 'nonresponsive' at Ah locus. Cancer Res 38:2777-2783.

Krahn D, Heidelberger C. 1977. Liver homogenate mediated mutagenesis in Chinese hamster V-79 cells by polycyclic aromatic hydrocarbons and aflatoxins. Mutat Res 46:27-44.

Lee RF, Sauerheber R, Dobbs GD. 1972. Uptake, metabolism, and discharge of polycyclic aromatic hydrocarbons by marine fish. Mar Biol 17:201-208 (as cited in Eisler 1987).

Lenson N. 1956. Multiple cutaneous carcinoma after creosote exposure. N Eng J Med 254:520-523.

Leversee GJ, Geisy JP, Landrum PF, et al. 1981. Disposition of benzo[a]pyrene in aquatic systems components: Periphyton, chironomids, daphnia, fish. In: Cooke M, Dennis AJ, eds. Chemical Analysis and Biological Fate: Polynuclear Aromatic Hydrocarbons. Fifth International Symposium. Battelle Press, Columbus, Ohio, pp. 357-366.

Levin W, Thakker DR, Wood AW, et al. 1978. Evidence that benzo[a]anthracene 3,4-diol-1,2-epoxide is an ultimate carcinogen on mouse skin. Cancer Res 38:1705-1710.

* Levin W, Wood A, Chang RL, et al. 1982. Oxidative metabolism of polycyclic aromatic hydrocarbons to ultimate carcinogens. Drug Metab Rev 13:555-580.

* Lindstedt G, Sollenberg J. 1982. Polycyclic aromatic hydrocarbons in the occupational environment. Scan J Work Environ Health 8:1-19.

Lloyd JW. 1971. Long-term mortality study of steelworkers. V. Respiratory cancer in coke plant workers. J Occup Med 13:53-68.

Lu P-Y, Metcalf RL, Plummer N, Mandel D. 1977. The environmental fate of three carcinogens: benzo[a]pyrene, benzidine, and vinyl chloride evaluated in laboratory model ecosystems. Arch Environ Contam Toxicol 6:129-142.

Maclure KM, MacMahon B. 1980. An epidemiologic perspective of environmental carcinogenesis. Epidemiol Rev 2:19-48.

Mahlum DD, Wright CW, Chess EK, Wilson BW. 1984. Fractionation of skin tumor-initiating activity in coal liquids. Cancer Res 44:5176-5181.

Marquardt H, Heidelberger C. 1972. Influence of "feeder cells" and inducers and inhibitors of microsomal mixed-function oxidases on hydrocarbon-induced malignant transformation of cells derived from C3H mouse prostate. Cancer Res 32:721-725.

Marquardt H, Baker S, Tierney B, Grover PL, Sims P. 1979. Comparison of mutagenesis and malignant transformation by dihydrodiols from benz[a]anthracene and 7,12-dimethylbenz[a]anthracene. Br J Cancer 39:540-547.

Martin CN, McDermid AC, Garner RC. 1978. Testing of known carcinogens and non-carcinogens for their ability to induce unscheduled DNA synthesis in HeLa cells. Cancer Res 38:2621-2627.

Matsumoto H, Kashimoto T. 1985. Average daily respiratory intake of polycyclic aromatic hydrocarbons in ambient air determined by capillary gas chromatography. Bull Environ Contam Toxicol 34:77-13

Mazumdar S, Redmond CK, Sollecito W, Sussman N. 1975. An epidemiological study of exposure to coal tar pitch volatiles among coke oven workers. J Air Pollut Control Assoc 25:382-389.

McCann J, Choi E, Yamasaki E, Ames BN. 1975. Detection of carcinogenesis as mutagens in the *Salmonella*/microsome test: Assay of 300 chemicals. Proc Natl Acad Sci USA 72:5135-5139.

McNeil D. 1983. Tar and pitch. In: Kirk-Othmer Encyclopedia of Chemical Technology. Vol. 22. 3rd ed. John Wiley and Sons, New York, pp. 564-600.

Medinsky MA, Kampcik SJ. 1985. Pulmonary retention of [^{14}C] benzo[a]pyrene in rats as influenced by the amount instilled. Toxicology 35:327-336.

Merck Index. 1983. An Encyclopedia of Chemicals, Drugs, and Biologicals. 10th ed. Merck and Company, Rahway, N.J.

Modica R, Fiume M, Bartosek I. 1982. Gas-liquid chromatographic assay of polycyclic aromatic hydrocarbon mixtures: Specifically modified method for rat tissues. J Chromatogr 24:352-355.

* Modica R, Fiume M, Guaitani A, Bartosek I. 1983. Comparative kinetics of benz[a]anthracene, chrysene, and triphenylene in rats after oral administration. I. Study with single compounds. Toxicol Lett 18:103-109.

Mushtaq M, Weems HB, Yang SK. 1986. Metabolic and stereoselective formation of non-K-region benz[a]anthracene 8,9- and 10,11-epoxides. Arch Biochem Biophys 246:478-487.

* Mushtaq M, Baq Z, Yang SK. 1987. Reversed-phase high performance liquid chromatographic separation of phenolic derivatives of benzo[a]pyrene, benz[a]anthracene, and chrysene with monomeric and polymeric C_{18} columns. J Chromatogr 385:293-298.

* NAS (National Academy of Sciences). 1972. Particulate Polycyclic Organic Matter. National Academy of Sciences, Washington, D.C.

NIOSH (National Institute for Occupational Safety and Health). 1977. Criteria for a Recommended Standard ... Occupational Exposure to Coal Tar Products. DHEW (NIOSH) Publication 78-107.

NIOSH (National Institute for Occupational Safety and Health). 1984. NIOSH Manual of Analytical Methods. 3rd ed. NIOSH, Cincinnati, Ohio.

Neal J, Rigdon RH. 1967. Gastric tumors in mice fed benzo[a]pyrene: A quantitative study. Toxicol Rep Biol Med 25:553-557.

Nesnow S, Heidelberger C. 1976. The effect of modifiers of microsomal enzymes on chemical oncogenesis in cultures of C3H mouse cell lines. Cancer Res 36:1801-1808.

NYSDEC (New York State Department of Environmental Conservation). 1984. Ambient Water Quality Criteria. Memo to Regional Water Engineers, Bureau Directors, and Section Chiefs. May 10, 1984.

OSHA (Occupational Safety and Health Administration). 1985. Permissible Exposure Limits. Code of Federal Regulations 29: 1910.1002.

O'Donovan WJ. 1920. Epitheliomatous ulceration among tar workers. Br J Dermatol Syphilis 32:215-252.

Ogan K, Katz E, Slavin W. 1979. Determination of polycyclic aromatic hydrocarbons in aqueous samples by reversed-phase liquid chromatography. Anal Chem 51:1315-1320.

Pal K. 1981. The induction of sister-chromatid exchanges in Chinese hamster ovary cells by K-region epoxides and some dihydrodiols derived from benz[a]anthracene, dibenz[a,c]anthracene, and dibenz[a,h]anthracene. Mutat Res 84:389-398.

Peter S, Palme GE, Rohrborn G. 1979. Mutagenicity of polycyclic hydrocarbons. III. Monitoring genetic hazards of benz[a]anthracene. Acta Morphol Acad Sci Hung 27:199-204.

Pienta RJ, Poiley JA, Lebherz WB, III. 1977. Morphological transformation of early passage golden Syrian hamster embryo cells derived from cryopreserved primary cultures as a reliable in vitro bioassay for identifying diverse carcinogens. Int J Cancer 19:642-655.

Poirier LA, de Serres FJ. 1979. Initial National Cancer Institute studies on mutagenesis as a prescreen for chemical carcinogens: An appraisal. J Natl Cancer Inst 62(4):919-926.

Pott P. 1775. Surgical observations relative to the cancer of the scrotum. London. Reprinted in Nat Cancer Inst Monogr 10:7-13 (1973).

Probst GS, McMahon RE, Hill LE, Thompson CZ, Epp JK, Neal SB. 1981. Chemically-induced unscheduled DNA synthesis in primary rat hepatocyte cultures: A comparison with bacterial mutagenicity using 218 compounds. Environ Mutagenesis 3:11-32.

Purde M, Etlin S. 1980. Cancer cases among workers in the Estonia oil shale processing industry. In: Rom WN, Archer VE, eds. Health Implications of New Energy Technologies. Ann Arbor Science, Ann Arbor, Mich., pp. 527-528.

* Randerath K, Randerath E, Agrawal HP, Gupta RC, Schurdak ME, Reddy MV. 1985. Postlabeling methods for carcinogen-DNA adduct analysis. Environ Health Perspect 62:57-65.

Randerath E, Avitts TA, Reddy MV, Miller RH, Everson RB, Randerath K. 1986. Comparative ^{32}P-analysis of cigarette smoke-induced DNA damage in human tissues and mouse skin. Cancer Res 46:5869-5877.

Redmond CK, Ciocco A, Lloyd JW, Rush HW. 1972. Long-term mortality study of steelworkers. VI. Mortality from malignant neoplasms among coke oven workers. J Occup Med 14:621-629.

Riggin R, Strup PE. 1984. Screening Methods for PAH Priority Pollutants in Wastewater. Prepared for the Environmental Monitoring Support Laboratory, Environmental Protection Agency, Cincinnati, Ohio, March 1984, EPA 600/S4-84-007.

Rocchi P, Ferreri AM, Borgia R, Proli G. 1980. Polycyclic hydrocarbon induction of diptheria toxin-resistant mutants in human cells. Carcinogenesis 1:765-767.

Rosenkranz HS, Poirier LA. 1979. Evaluation of the mutagenicity and DNA-modifying activity of carcinogens and non-carcinogens in microbial systems. J Natl Cancer Inst 62:873-892.

Roszinsky-Kocher G, Basler A, Rohrborn G. 1979. Mutagenicity of polycyclic hydrocarbons. V. Induction of sister-chromatid exchanges in vivo. Mutat Res 66:65-67.

San RHC, Stich HF. 1975. DNA repair synthesis of cultured human cells as a rapid bioassay for chemical carcinogens. Int J Cancer 16:284-291.

* Sanders CL, Skinner C, Gelman RA. 1986. Percutaneous absorption of 7,10 ^{14}C-benzo[a]pyrene and 7,12 ^{14}C-dimethylbenzo[a]pyrene in mice. JEPTO 2:25-34.

Santodonato J, Howard P, Basu D. 1981. Health and ecological assessment of polynuclear aromatic hydrocarbons. J Environ Pathol Toxicol 5:51-75.

Sawicki E. 1976. Analysis of Atmospheric Carcinogens and Their Cofactors. INSERM Symposia Series. Vol. 52, pp. 297-354.

Schlede E, Kuntzman R, Haber S, Conney AH. 1970a. Effect of enzyme induction on the metabolism and tissue distribution of benzo[a]pyrene. Cancer Res 30:2893-2897.

Schlede E, Kuntzman R, Coney AH. 1970b. Stimulating effect of benzo[a]pyrene and phenobarbital pretreatment on the biliary excretion of benzo[a]pyrene metabolites in the rats. Cancer Res 30:2898-2904.

Schottenfeld D, Fraumeni JF, Jr. eds. 1982. Cancer Epidemiology and Prevention. W.B. Sanders Co., Philadelphia, Pa.

Sellakumar A, Stenback F, Rowland J. 1976. Effects of different dusts on respiratory carcinogenesis in hamsters induced by benzo[a]pyrene and diethylnitrosamine. Europ J Cancer 12:313-319.

Simmon VF. 1979a. In vitro assays for recombinogenic activity of chemical carcinogens and related compounds with *Saccharomyces cerevisiae* D3. J Natl Cancer Inst 62:901-909.

Simmon VF. 1979b. In vitro mutagenicity of chemical carcinogens and related compounds with *Salmonella typhimurium*. J Natl Cancer Inst 62(4):893-899.

Simmon VF, Rosenkranz HS, Zeiger E, Poirier LA. 1979. Mutagenic activity of chemical carcinogens and related compounds in the intraperitoneal host-mediated assay. J Natl Cancer Inst 62(4):911-918.

* Sims P, Grover PL. 1974. Epoxides in polycyclic aromatic hydrocarbon metabolism and carcinogenesis. Adv Cancer Res 20:165-274.

Sims P, Grover PL. 1981. Involvement of dihydrodiols and diol-epoxides in the metabolic activation of polycyclic hydrocarbons other than benzo[a]pyrene. In: Gelboin HV, Ts'O POP, eds. Polycyclic Hydrocarbons and Cancer. Vol. 3. Academic Press, New York, pp. 117-181.

Sims P. 1982. The metabolic activation of some polycyclic hydrocarbons: The role of dihydrodiols and diol epoxides. Adv Exp Med Biol 136:487-500.

Slaga TJ, Humberman E, Selkirk JK, Harvey RG, Bracken WM. 1978. Carcinogenicity and mutagenicity of benz[a]anthracene diols and diol-epoxides. Cancer Res 38:1699-1704.

Slaga TJ, diGiovanni J. 1984. Inhibition of chemical carcinogenesis. In: Searle CE, ed. Chemical Carcinogens. 2nd ed. Vol.2. ACS Monograph 182. Washington, DC.

Sorrell RK, Brass HJ, Reding R. 1981. A Review of Occurrences and Treatment of Polynuclear Aromatic Hydrocarbons. EPA-600/0-81-066.

Stenback F, Rowland J. 1979. Experimental respiratory carcinogenesis in hamsters: environmental, physicochemical, and biological aspects. Oncol 36:63-71.

Stenback F, Rowland J, Sellakumar A. 1976. Carcinogenicity of benzo[a]pyrene and dusts in the hamster lung (instilled intratracheally with titanium oxide, aluminum oxide, carbon, and ferric oxide). Oncol 33:29-34.

Stich HF, San RHC. 1973. DNA repair synthesis and survival of repair deficient human cells exposed to the K-region epoxide of benz[a]anthracene. Proc Soc Exp Biol Med 142:155-158.

Sugiyama T. 1973. Chromosomal aberrations and carcinogenesis by various benz[a]anthracene derivatives. Gann 64:637-639.

Thakker DR, Levin W, Yagi H, 1982. Stereoselective metabolism of the (+) and (-) enantiomers of trans-3,4-dihydroxy-3,4-dihydrobenz[a]anthracene by rat liver microsomes and by a purified and reconstituted cytochrome P-450 system. J Biol Chem 257:5103-5110.

Thyssen J, Althoff J, Kimmerle G, Mohr U. 1981. Inhalation studies with benzo[a]pyrene in Syrian golden hamsters. J Natl Cancer Inst 66:575-577.

Tong C, Laspia MF, Telang S, Williams GM. 1981a. The use of adult rat liver cultures in the detection of the genotoxicity of various polycyclic aromatic hydrocarbons. Environ Mutagenesis 3:477-487.

Tong C, Ved Brat S, Williams GM. 1981b. Sister-chromatid exchange induction by polycyclic aromatic hydrocarbons in an intact cell system of adult rat-liver epithelial cells. Mutat Res 91:467-473.

Tornquist A, Wiklund L, Toftgard R. 1985. Investigation of absorption, metabolism kinetics, and DNA-binding of intratracheally administered benzo[a]pyrene in the isolated, perfused rat lung: A comparative study between microcrystalline and particulate absorbed benzo[a]pyrene. Chem Biol Interact 54:185-198.

USDOC (U.S. Department of Commerce). 1986. U.S. Imports for Consumption and General Imports. FT 246/Annual 1985.

Ved Brat S, Tong C, Telang S, Williams GM. 1983. Comparison of sister chromatid exchange and mammalian cell mutagenesis at the hypoxanthine guanine phosphoribosyl transferase locus in adult rat liver epithelial cells. Ann NY Acad Sci 407:474-475.

Verschueren K. 1983. Handbook of Environmental Data on Organic Chemicals. 2nd ed. Van Nostrand Reinhold, New York.

* Vo-Dinh T, Tromberg BJ, Griffin GD, Ambrose KR, Sepaniak MJ, Gardenhire EM. 1987. Antibody-based fiberoptics biosensor for the carcinogen benzo[a]pyrene. Appl Spectrosc 41:735-738.

View Database. 1989. Agency for Toxic Substances and Disease Registry (ATSDR), Division of Health Studies, Atlanta, Ga., Nov. 8, 1989.

Wallace WE, Keane MJ, Hill CA, Xu J, Ong T. 1987. Mutagenicity of diesel exhaust particles and oil shale particles dispersed in lecithin surfactant. J Toxicol Environ Health 21:163-171.

* Wang DT, Meresz O. 1982. Occurrence and potential uptake of polynuclear aromatic hydrocarbons of highway traffic origin by proximally grown food crops. In: Cooke M, Dennis AS, Fisher GL, eds. Polynuclear Aromatic Hydrocarbons: Physical and Biological Chemistry: Sixth International Symposium. Battelle Press, Columbus, Ohio, pp. 885-896.

Waters MD, Stack HF, Brady AL, Lohman PH, Haroun L, Vainio H. 1987. Use of computerized data listings and activity profiles for genetic and related effects in the review of 195 compounds. Genetic Toxicology Division, Health Effects Research Laboratory, Environmental Protection Agency, Research Triangle Park, N.C.

Weibel FJ. 1980. Activation and inactivation of carcinogens by microsomal monooxygenases: Modification by benzoflavones and polycyclic aromatic hydrocarbons. In: Slaga TJ, ed. Carcinogenesis. Vol. 5. Modifiers of Chemical Carcinogenesis. Raven Press, New York.

Williams GM. 1977. Detection of chemical carcinogens by unscheduled DNA synthesis in rat primary cell cultures. Cancer Res 37:1845-1851.

Wise SA, Benner BA, Chesler SN, et al. 1986. Characterization of the polycyclic aromatic hydrocarbons from two standard reference material air particulate samples. Anal Chem 58:3067-3077.

Wislocki PG, Kapitulnik J, Levin W, et al. 1978. Exceptional carcinogenic activity of benzo[a]anthracene 3,4-dihydrodiol in the newborn mouse and the bay-region theory. Cancer Res 38:693-696.

Wood AW, Levin W, Lu AYH, et al. 1976. Mutagenicity of metabolically activated benz[a]anthracene-3,4-dihydrodiol. Evidence of bay region activation of carcinogenic polycyclic hydrocarbons. Biochem Biophys Res Commun 72:680-686.

Wood AW, Levin W, Chang RL, et al. 1977a. Tumorigenicity of five dihydrodiols of benz[a]anthracene on mouse skin: Exceptional activity of benz[a]anthracene-3,4-dihydrodiol. Proc Natl Acad Sci USA 74:3176.

Wood AW, Chang RL, Levin W, et al. 1977b. Mutagenicity and cytotoxicity of benz[a]anthracene diol-epoxides and tetrahydroepoxides. Exceptional activity of the bay region 1,2-epoxides. Proc Natl Acad Sci USA 74:2746-2750.

WHO (World Health Organization). 1971. International Standards for Drinking Water. 3rd ed. World Health Organization, Geneva, Switzerland.

Wynder EL, Hoffmann D. 1967. Tobacco and Tobacco Smoke. Academic Press, New York.

Yang SK, Weems HB, Mustag M. 1984. Direct resolution of mono- and diol enantiomers of unsubstituted and methyl-substituted benz[a]anthracene and benzo[a]pyrene by high-performance liquid chromatography with a chiral stationary phase. J Chromatogr 316:569-584.

Zijlstra JA, Vogel EW. 1984. Mutagenicity of 7,12-dimethylbenz(a)-anthracene and some other aromatic mutagens in *Drosophila melanogaster*. Mutat Res 125:243-261.

11. GLOSSARY

Acute Exposure--Exposure to a chemical for a duration of 14 days or less, as specified in the Toxicological Profiles.

Bioconcentration Factor (BCF)--The quotient of the concentration of a chemical in aquatic organisms at a specific time or during a discrete time period of exposure divided by the concentration in the surrounding water at the same time or during the same time period.

Carcinogen--A chemical capable of inducing cancer.

Ceiling value (CL)--A concentration of a substance that should not be exceeded, even instantaneously.

Chronic Exposure--Exposure to a chemical for 365 days or more, as specified in the Toxicological Profiles.

Developmental Toxicity--The occurrence of adverse effects on the developing organism that may result from exposure to a chemical prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism.

Embryotoxicity and Fetotoxicity--Any toxic effect on the conceptus as a result of prenatal exposure to a chemical; the distinguishing feature between the two terms is the stage of development during which the insult occurred. The terms, as used here, include malformations and variations, altered growth, and in utero death.

Frank Effect Level (FEL)--That level of exposure which produces a statistically or biologically significant increase in frequency or severity of unmistakable adverse effects, such as irreversible functional impairment or mortality, in an exposed population when compared with its appropriate control.

EPA Health Advisory--An estimate of acceptable drinking water levels for a chemical substance based on health effects information. A health advisory is not a legally enforceable federal standard, but serves as technical guidance to assist federal, state, and local officials.

Immediately Dangerous to Life or Health (IDLH)--The maximum environmental concentration of a contaminant from which one could escape within 30 min without any escape-impairing symptoms or irreversible health effects.

Intermediate Exposure--Exposure to a chemical for a duration of 15-364 days, as specified in the Toxicological Profiles.

Immunologic Toxicity--The occurrence of adverse effects on the immune system that may result from exposure to environmental agents such as chemicals.

In vitro--Isolated from the living organism and artificially maintained, as in a test tube.

In vivo--Occurring within the living organism.

Key Study--An animal or human toxicological study that best illustrates the nature of the adverse effects produced and the doses associated with those effects.

Lethal Concentration(LO) (LC_{LO})--The lowest concentration of a chemical in air which has been reported to have caused death in humans or animals.

Lethal Concentration(50) (LC_{50})--A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

Lethal Dose(LO) (LD_{LO})--The lowest dose of a chemical introduced by a route other than inhalation that is expected to have caused death in humans or animals.

Lethal Dose(50) (LD_{50})--The dose of a chemical which has been calculated to cause death in 50% of a defined experimental animal population.

Lowest-Observed-Adverse-Effect Level (LOAEL)--The lowest dose of chemical in a study or group of studies which produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.

Lowest-Observed-Effect Level (LOEL)--The lowest dose of chemical in a study or group of studies which produces statistically or biologically significant increases in frequency or severity of effects between the exposed population and its appropriate control.

Malformations--Permanent structural changes that may adversely affect survival, development, or function.

Minimal Risk Level--An estimate of daily human exposure to a chemical that is likely to be without an appreciable risk of deleterious effects (noncancerous) over a specified duration of exposure.

Mutagen--A substance that causes mutations. A mutation is a change in the genetic material in a body cell. Mutations can lead to birth defects, miscarriages, or cancer.

Neurotoxicity--The occurrence of adverse effects on the nervous system following exposure to a chemical.

No-Observed-Adverse-Effect Level (NOAEL)--That dose of chemical at which there are no statistically or biologically significant increases in frequency or severity of adverse effects seen between the exposed population and its appropriate control. Effects may be produced at this dose, but they are not considered to be adverse.

No-Observed-Effect Level (NOEL)--That dose of chemical at which there are no statistically or biologically significant increases in frequency or severity of effects seen between the exposed population and its appropriate control.

Permissible Exposure Limit (PEL)--An allowable exposure level in workplace air averaged over an 8-h shift.

$q1^*$--The upper-bound estimate of the low-dose slope of the dose-response curve as determined by the multistage procedure. The $q1^*$ can be used to calculate an estimate of carcinogenic potency, the incremental excess cancer risk per unit of exposure (usually $\mu g/L$ for water, mg/kg/day for food, and $\mu g/m^3$ for air).

Reference Dose (RfD)--An estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure of the human population to a potential hazard that is likely to be without risk of deleterious effects during a lifetime. The RfD is operationally derived from the NOAEL (from animal and human studies) by a consistent application of uncertainty factors that reflect various types of data used to estimate RfDs and an additional modifying factor, which is based on a professional judgment of the entire database on the chemical. The RfDs are not applicable to nonthreshold effects such as cancer.

Reportable Quantity (RQ)--The quantity of a hazardous substance that is considered reportable under CERCLA. Reportable quantities are: (1) 1 lb or greater or (2) for selected substances, an amount established by regulation either under CERCLA or under Sect. 311 of the Clean Water Act. Quantities are measured over a 24-h period.

Reproductive Toxicity--The occurrence of adverse effects on the reproductive system that may result from exposure to a chemical. The toxicity may be directed to the reproductive organs and/or the related endocrine system. The manifestation of such toxicity may be noted as alterations in sexual behavior, fertility, pregnancy outcomes, or modifications in other functions that are dependent on the integrity of this system.

Short-Term Exposure Limit (STEL)--The maximum concentration to which workers can be exposed for up to 15 min continually. No more than four excursions are allowed per day, and there must be at least 60 min between exposure periods. The daily TLV-TWA may not be exceeded.

Target Organ Toxicity--This term covers a broad range of adverse effects on target organs or physiological systems (e.g., renal, cardiovascular) extending from those arising through a single limited exposure to those assumed over a lifetime of exposure to a chemical.

Teratogen--A chemical that causes structural defects that affect the development of an organism.

Threshold Limit Value (TLV)--A concentration of a substance to which most workers can be exposed without adverse effect. The TLV may be expressed as a TWA, as a STEL, or as a CL.

Time-weighted Average (TWA)--An allowable exposure concentration averaged over a normal 8-h workday or 40-h workweek.

Uncertainty Factor (UF)--A factor used in operationally deriving the RfD from experimental data. UFs are intended to account for (1) the variation in sensitivity among the members of the human population, (2) the uncertainty in extrapolating animal data to the case of humans, (3) the uncertainty in extrapolating from data obtained in a study that is of less than lifetime exposure, and (4) the uncertainty in using LOAEL data rather than NOAEL data. Usually each of these factors is set equal to 10.

APPENDIX: PEER REVIEW

A peer review panel was assembled for benz[a]anthracene. The panel consisted of the following members: Dr. Roger O. McClellan, Lovelace Inhalation Toxicology Research Institute; Dr. Dietrich Hoffmann, Naylor Dana Institute for Disease Prevention; and Dr. Alexander Wood, Roche Institute of Molecular Biology. These experts collectively have knowledge of B[a]A's physical and chemical properties, toxicokinetics, key health end points, mechanisms of action, human and animal exposure, and quantification of risk to humans. All reviewers were selected in conformity with the conditions for peer review specified in the Superfund Amendments and Reauthorization Act of 1986, Section 110.

A joint panel of scientists from ATSDR and EPA has reviewed the peer reviewers' comments and determined which comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound. A list of databases reviewed and a list of unpublished documents cited are also included in the administrative record.

The citation of the peer review panel should not be understood to imply their approval of the profile's final content. The responsibility for the content of this profile lies with the Agency for Toxic Substances and Disease Registry.